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JOURNAL OF GENERAL CHEMISTRY

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A STUDY OF THE EQUILIBRIUM OF TWO LIQUID PHASES IN
THE SYSTEM OF n-HEXANE–NITROBENZENE–ANILINE

N. I. Nikurashina, R. V. Mertslin and G. M. Komarova

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The problems of practical importance in the extraction of substances from solutions, layering out of a solution of two miscible liquids by salting out, drying of solutions and other similar situations are connected with the problem of the distribution of a third substance between two liquids which are either insoluble in each other or are but partly soluble.

As shown by an extensive experimental material, the Nernst distribution law is applicable only to ideal solutions and does not consider the possible change of the component proportions with change of the content of the third component in the mixtures.

Since the problem of the distribution of the third component between two equilibrium phases is related to the equilibrium of two liquid phases in three-component systems, it is evident that the rules which exist in such systems would aid the more correct approach to the solution of the given problem.

D. N. Tarasenkov [1, 2] devoted himself to the study of the distribution of a substance between liquid phases by examination of the node locations within the layering-out region. The substance of the rule found by him consists of the statement that "if one extends the nodes, i.e., lines which connect the compositions of conjugated solutions, these extended lines will intersect at one point which lies on the extension of one of the sides of the composition triangle". The nodal intersection occurs at the apex of the composition triangle for systems with two binary layers. The Tarasenkov rule does not provide a general rule for the distribution of a substance between two liquid phases and for the location of the node system.

Some rules of the node distribution in the region of two-phase liquid equilibrium in three-component systems were established by R. V. Mertslin [3]. He showed that the character of the binodal curve and the node distribution in the layering-out region are mutually interconnected.

Let the composition triangle ABS (Fig. 1) have a region of layering-out $l_{CB}Kl_{BC}$. The critical point is turned toward side AB, showing of the subordinate character of the former. Actually, the layering-out region will touch side AB by its critical point K with alteration of the equilibrium conditions, i.e., system AB will become a layered system. On this basis the binary system toward which the critical point is turned is regarded as the dependent one, while the other homogeneous binary system AC is regarded as the predominant one. Extensive experimental material showed that if the critical point K is turned toward the left boundary of the homogeneous system, the nodes l_2l_1 would have a right-handed directivity, i.e., will pass to the right of the section Bm. If the critical point on the binodal curve (Fig. 2) points toward the right boundary of the binary system BC, the nodes would have the left directivity. This rule remains in force even in the case in which the layering-out region spreads from one side of the composition triangle to the other side. In reality, we can see by extrapolating the binodal curve on Fig. 3, that its critical point K is the imaginary region and is placed to the right of AB; hence, nodes l_2l_1 will have the left directivity. In more complex cases which a chemical compound V would form in the predominant system AC, this compound being of the daltonide type with maximum (Fig. 4) or minimum (Fig. 5) solubility in component B, the node directivity for the region of the composition diagram which lies on both sides of the quasi-binary section BV will be quite definite, which can be seen in Figures 4 and 5.
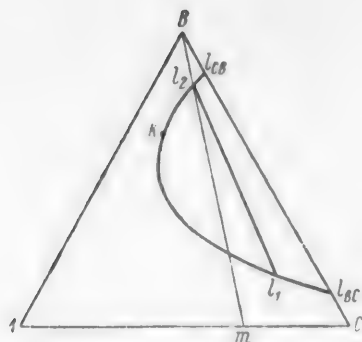
Fig. 1. Explanation in the text.
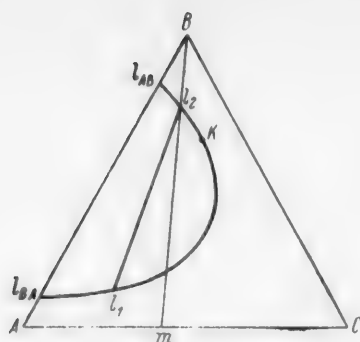
Fig. 2. Explanation in the text.

The change of node directivity may occur only through the node of zero directivity which under any temperature conditions should coincide with the line of the quasi-binary section BV. The ends of this node are singular points on the binodal solubility curves.
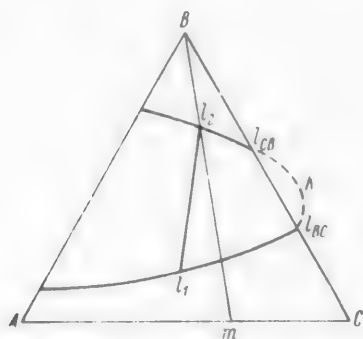
Fig. 3. Explanation in the text.
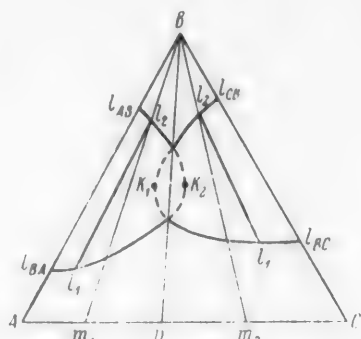
Fig. 4. Explanation in the text.

The aim of this work was the experimental confirmation of the rule of node disposition in the system of n-hexane—aniline—nitrobenzene.
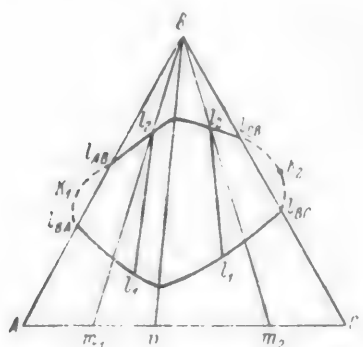
Fig. 5. Explanation in the text.
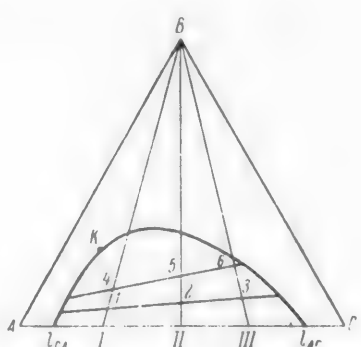
Fig. 6. Explanation in the text.

EXPERIMENTAL

The following substances were taken for the study: n-hexane, redistilled, b.p. 69°; nitrobenzene prepared by Gattermann technique, purified, redistilled, b.p. 206°; aniline, purified, twice redistilled, b.p. 184.0°.
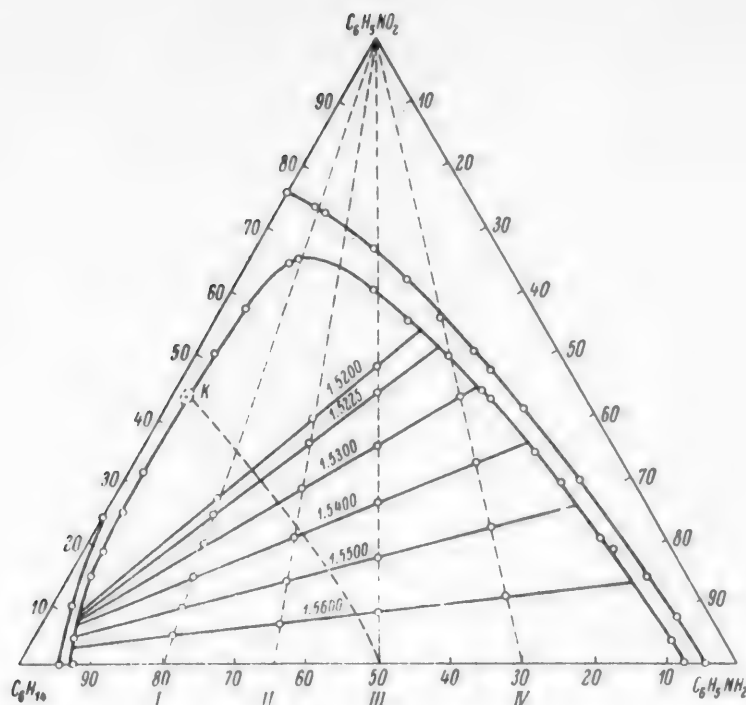
Fig 7. Composition diagram of the system hexane–nitrobenzene–aniline.

The study of the equilibrium of two liquid phases was done by the Bancroft's isothermic titration method and by the section method.
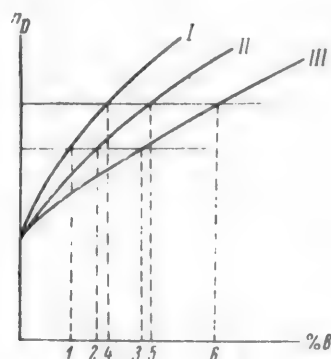
Fig. 8. Explanation in the text.

The method of isothermic titration has been described in detail in the literature. It consists of a visual observation of the phase transition after the addition to the initial mixture of a third component with which the titration is performed.

The section method was developed by Mertslin [3, 4] as a method of determination of the composition

Fig. 9. Index of refraction of nitro-benzene layers for sections I – IV.

of two equilibrium phases in three-component systems and has the advantage over the method of Schreinemaker which proposes to determine the compositions of conjugated phases by a graphical analytical method. The section method is based on the possibility of finding the composition of the conjugated layer from the concentration of one component in it and the method permits one to determine the location of the entire node and not only its terminal values.

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TABLE 1

Compositions of Mixtures which Correspond to Points on Binodal Curve at 20°

No. of expt.	Content of components in the mixtures (in weight %)		
	hexane	aniline	nitroben-zene
1	6.60	89.60	3.80
2	90.30	5.40	4.30
3	81.10	4.70	14.20
4	79.00	3.10	17.90
5	7.90	73.90	18.20
6	9.10	68.90	22.00
7	73.00	2.60	24.40
8	9.90	61.20	28.90
9	61.10	7.60	31.30
10	11.60	54.80	33.60
11	13.00	44.50	42.50
12	13.50	42.50	44.00
13	15.50	35.20	49.30
14 *	47.50	0.90	51.60
15	18.20	26.60	55.20
16 **	41.60	2.10	56.30
17	20.90	19.30	59.80
18	30.50	5.30	64.20
19	28.40	6.40	65.20

TABLE 2

Composition of Mixtures which Correspond to Points on Binodal Curve at 10°

Content of components in mixtures (in weight %)		
hexane	aniline	nitroben-zene
5.10	87.50	7.40
6.00	79.10	14.90
7.40	62.90	29.70
9.00	50.50	40.50
7.00	51.60	41.40
11.20	41.80	47.00
11.80	37.90	50.30
13.60	30.80	55.50
15.50	22.70	61.80
17.10	15.90	67.00
21.20	5.90	72.90
22.10	4.50	73.40

TABLE 3

Indexes of Refraction of Ternary Mixtures

Section I $[C_6H_5NH_2]:[C_6H_{14}]=20:80$		Section II $[C_6H_5NH_2]:[C_6H_{14}]=35:65$		Section III $[C_6H_5NH_2]:[C_6H_{14}]=50:50$		Section IV $[C_6H_5NH_2]:[C_6H_{14}]=70:30$	
n^{20}	content nitrobenzene (wt. %)	n^{20}	content nitrobenzene (wt. %)	n^{20}	content nitrobenzene (wt. %)	n^{20}	content nitrobenzene (wt. %)
1.5698	0.00	1.5695	0.00	1.5698	0.00	1.5698	0.00
1.5585	5.45	1.5580	8.50	1.5610	8.32	1.5605	10.50
1.5540	7.50	1.5525	12.30	1.5580	10.00	1.5548	16.00
1.5450	11.50	1.5465	16.00	1.5525	15.00	1.5520	19.50
1.5380	15.00	1.5400	20.00	1.5465	20.00	1.5485	23.50
1.5365	16.10	1.5360	23.25	1.5350	29.60	1.5465	25.00
1.5285	20.00	1.5340	25.15	1.5338	30.50	1.5410	30.80
1.5230	24.40	1.5320	27.00	1.5300	34.50	1.5340	39.28
1.5148	29.95	1.5230	35.00	1.5270	38.48	1.5300	43.00
1.5055	37.00	1.5165	42.50	1.5225	43.00	1.5288	45.12
1.5010	41.50	1.5157	45.50	1.5210	45.00		
1.4940	50.00	1.5125	50.00				

TABLE 4

Node	Index of refraction corresponding to the node	Content of nitrobenzene in mixtures of the sections (wt.%)			
		I	II	III	IV
1	1.5600	4.50	6.50	8.50	11.00
2	1.5500	9.00	13.50	17.00	21.50
3	1.5400	14.00	20.00	25.00	32.00
4	1.5300	19.50	28.50	34.50	43.00
5	1.5220	23.50	35.50	43.00	
6	1.5200	26.00	38.00	47.50	

* Weak critical opalescence.

** Critical opalescence.

Let us cut the layered region (Fig. 6) on the composition triangle by sections I, II and III, each of which is characterized by the invariant ratio of components A and C. A series of mixtures is prepared for each section, these mixtures being located within the layered-out region and differing from each other in the content of component B. After the establishment of equilibrium, the indexes of refraction of one of the liquid phases are measured and, for each section, a graph is constructed showing the functional dependence of the index of refraction and the percentage content of component B in the mixtures. For the determination of node positions in the layered-out region it is necessary to draw a series of straight lines on the functional curves (Fig. 8) these lines corresponding to a definite index of refraction. Points 1-3 or 4-6 will indicate the percentage content of component B in the mixtures which lie on the same node. The corresponding points are placed onto the plane of the composition triangle, while the intersection of the straight line, which connects them with the binodal curve, will indicate the composition of the conjugated phases.

The measurements of the index of refraction were performed with the RLU refractometer of the Abbe type, using a thermostated setup.

The results of the isothermic titration are given in Tables 1 and 2, and in Figure 7.

An isothermic titration was run at 10° in order to clarify the change of the equilibrium picture with change in the temperature.

For the study of the equilibrium of two liquid phases by the section method we prepared mixtures containing aniline and hexane in a definite weight ratio with a variable amount of nitrobenzene.

The mixtures were weighed in glass ampuls, sealed, shaken thoroughly and thermostated at 20° until equilibrium was established (48 hours); index of refraction of the nitrobenzene layer was measured. The results are given in Table 3 and in Figure 9.

In Table 4, we give the data on the basis of which we constructed the nodes in the layered-out region (Fig. 7).

The critical point of the layered-out region points toward the system of hexane–nitrobenzene which indicates the subordinate nature of the interaction of these components. The binary system of nitrobenzene–aniline is the predominant system. We determined the node directivity by drawing a section line from the hexane apex to the predominant system. All nodes have the left directivity which confirms the R. V. Mertslin rule of node directivity which was formulated above.

SUMMARY

1. The system n-hexane–nitrobenzene–aniline was studied via solubility at 10° and 20°. It was shown that the critical point is directed toward the system of n-hexane–nitrobenzene.

2. A system of nodes in the layered-out region was obtained by the use of R. V. Mertslin's method of sections.

3. It was shown that the node directivity in the layered-out region is in agreement with the R. V. Mertslin rule.

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[3] R. V. Mertslin, Bull. Acad. Sci. USSR, Div. Chem. Sci. No. 6, 1407 (1937).

[4] R. V. Mertslin, Bull. Perm Biological Research Institute 11, No. 1-2, 5 (1937).

A STUDY OF THE EQUILIBRIUM OF THREE LIQUID PHASES
IN A FOUR-COMPONENT SYSTEM OF WATER-n-HEXANE-
ANILINE-NITROBENZENE

N. I. Nikurashina, G. M. Komarova and R. V. Mertslin

Saratov State University

During the study of the equilibrium of two liquid phases in the system of hexane-aniline-nitrobenzene we showed experimentally the rule of the node distribution which is determined by the component interaction in the predominant binary system [1]. The present work is a further development of the predominance theory which is being considered in a more complex case of a four-component system of water-n-hexane-aniline-nitrobenzene.

Binary or ternary systems may be the predominant ones in four-component systems. Depending on this, the character of the establishment of the volume of the three liquid phases and its development may be different. Let us consider the case in which three liquid phases, starting from the ABD boundary, move inside the tetrahedron upon addition of the fourth component, do not reach the other boundary and are terminated by the critical node $l_1^i K_{23}$ (Fig. 1). A volume of three liquid phases is formed thereupon. The system BC is the sole predominant system in this case. The interaction among its components should be expressed not only at the surface of the two-phase states but also at the surface of the three-phase state and at the location of the critical node.

Let us consider the section $m_1 m_2 m_3$ of the tetrahedron ABCD which cuts the volume of the liquid phases, starting at the ABD boundary and terminating at the critical node $l_1' K_{23}$ inside the tetrahedron. The picture of the intersection resembles the one of equilibrium of two liquid phases in a three-component system (Fig. 2). Point K is the trace of the intersection of the section by the critical node $l_1' K_{23}$. Curve aKb delineates the equilibrium of three liquid phases while curve aK is the totality of points which originated in the intersection of the nodal sides $l_1 l_2$ of the triangles of the three liquid phases which participate in the volume of the three liquid phases. Curve Kb originated as a result of intersection of other nodal sides $l_3 l_1$ of the triangles of the three liquid phases by section $m_1 m_2 m_3$. Thus, the lines of intersection of the triangles of the three liquid phases will pass through the area delineated by curve aKb during the sectioning of the volume of the three liquid phases by section $m_1 m_2 m_3$. Let us denote by $M_1 M_2$ the line of intersection of one of the triangles of the three liquid phases by section $m_1 m_2 m_3$. This line of intersection plays the role of a node since it belongs to but one triangle of the three phases and the rules found for all lines of intersection of the triangles will apply also to the disposition of the triangles of the three liquid phases within the tetrahedron.

The direction of the nodal triangles in respect to the critical point K in section $m_1 m_2 m_3$ is determined similarly to the nodes of the region of binary layering-out as it is evident in Fig. 2 (b). The determination of the location of section of the nodal triangles (straight lines of $M_1 M_2$ type in horizontal sections) relative to the critical point would permit the extension of the predominance theory to the equilibrium of three liquid phases in four-component systems.

The aim of this work was the experimental confirmation of the rule about the direction of the nodal triangles of three liquid phases in the system of water-n-hexane-aniline-nitrobenzene.

Fig. 1. Explanation in the text.

Fig. 2. Explanation in the text.

EXPERIMENTAL
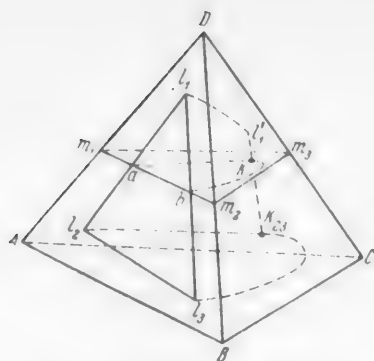
The following substances were taken for the study: n-hexane, distilled, b.p. 69°; nitrobenzene, prepared by the Gattermann technique, purified and distilled, b.p. 206°; aniline, purified and twice distilled, b.p. 184°; water, twice distilled.

The polythermic method of Alekseev and the section method of Mertslin were used in the study. The Alekseev method is being used widely and has been described in the literature. The section method was published [2] and described in detail [1]. Its substance consists of the construction of a node system from the data of measurement of some physical property of a phase depending on the concentration of one of the components in the mixtures.
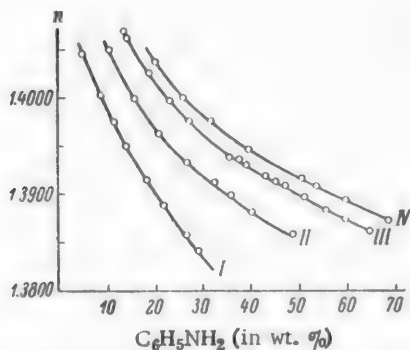
Fig. 3. Index of refraction of hexane layer in section with 75% H_2O. I) 70% hexane, II) 50% hexane, III) 30% hexane, IV) 20% hexane.

Fig. 4. Index of refraction of nitrobenzene layer in section with 75% H_2O. II) 50% hexane, III) 30% hexane, IV) 20% hexane.

Three horizontal sections in the tetrahedron with constant water content (75, 50 and 25 weight %) were studied by the section method during the study of equilibrium of three liquid phases. Several sections with constant hexane content were taken in each section. The mixtures were prepared in sealed glass ampuls and were kept in a thermostat at 20° until equilibrium was established. The index of refraction of one or of two layers was measured after 48 hours. The measurements were made with an RLU refractometer of Abbe type, using a thermostated setup. The index of refraction of the upper, hexane layer was measured for the section with 50% H_2O. Indexes of refraction of the hexane layer and of the middle layer, called the nitrobenzene layer, were measured for sections with 25 and 75% H_2O. The index of refraction of the aqueous layer varied but little for all the sections, and it was impossible to construct a functional dependence for this layer.

The results of measurements of the index of refraction are given in Figs. 3-7. Having constructed the curve of functional dependence of the index-of-refraction—percentage-content-of-aniline in the complexes

TABLE 1

Section With 75% H_2O, Hexane Layer

Node	n^{20}	Weight % of aniline in various sections with respect to hexane			
		70% C_6H_{14}	50% C_6H_{14}	30% C_6H_{14}	20% C_6H_{14}
1	1.4025	7.50	13.00	19.00	22.00
2	1.4000	9.50	16.00	22.50	25.80
3	1.3950	14.00	23.50	33.50	38.00
4	1.3925	17.50	29.00	40.50	46.50
5	1.3900	20.50	35.00	50.50	57.00
6	1.3875	24.00	41.50	58.00	66.00
		Nitrobenzene Layer			
1	1.5500	—	37.00	52.00	60.00
2	1.5400	—	28.50	39.00	75.00
3	1.5250	—	20.50	28.00	33.50
4	1.5200	—	18.00	25.50	29.50
5	1.5050	--	12.00	17.50	20.00

TABLE 2

Section with 50% H_2O, Hexane Layer

Node	n^{20}	Weight % of aniline for various sections with respect to hexane					
		70% C_6H_{14}	60% C_6H_{14}	50% C_6H_{14}	40% C_6H_{14}	30% C_6H_{14}	20% C_6H_{14}
1	1.4025	5.50	8.00	10.50	22.00	—	—
2	1.4000	7.00	9.50	12.50	15.30	—	21.00
3	1.3950	10.50	15.00	19.00	23.00	28.00	31.00
4	1.3900	17.00	23.00	29.00	34.50	41.00	47.00
5	1.3875	20.50	27.50	35.00	42.00	49.00	57.00
6	1.3850	25.00	33.50	42.50	50.50	59.00	67.50

TABLE 3

Section with 25% H_2O, Hexane Layer

Node	n^{20}	Weight % of aniline for various sections with respect to hexane					
		80% C_6H_{14}	70% C_6H_{14}	60% C_6H_{14}	50% C_6H_{14}	40% C_6H_{14}	30% C_6H_{14}
1	1.3950	6.00	10.50	15.50	20.00	25.00	30.00
2	1.3900	10.00	16.50	23.00	29.50	36.00	42.00
3	1.3875	12.50	20.50	28.00	35.50	43.00	51.00
4	1.3850	16.00	25.00	33.50	42.50	52.00	61.00
		Nitrobenzene Layer					
1	1.5150	4.50	8.00	12.00	15.80	—	—
2	1.5200	5.50	10.00	14.50	18.80	—	—
3	1.5350	9.50	16.00	21.80	28.00	—	—
4	1.5500	14.00	22.50	30.00	38.00	—	—
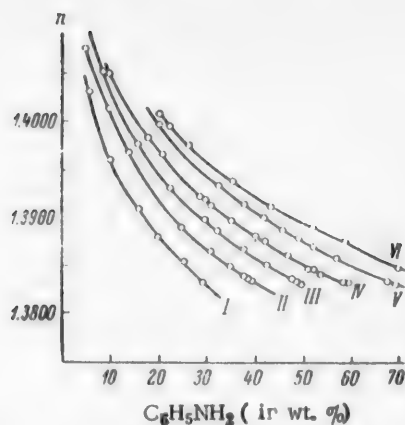
Fig. 5. Index of refraction of hexane layer in section with 50% H_2O. I) 70% hexane, II) 60% hexane, III) 50% hexane, IV) 40% hexane, V) 30% hexane, VI) 20% hexane.
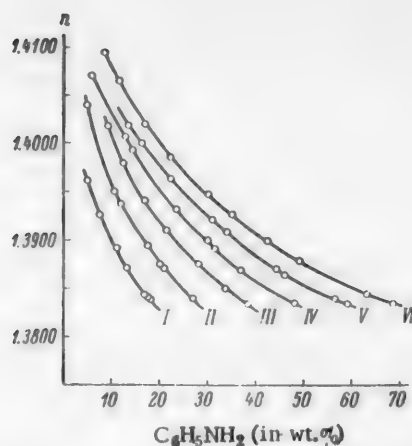
Fig. 6. Index of refraction of hexane layer in section with 25% H_2O. I) 80% hexane, II) 70% hexane, III) 60% hexane, IV) 50% hexane, V) 40% hexane, VI) 30% hexane.
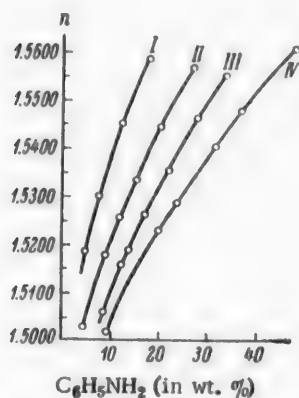
Fig. 7. Index of refraction of nitrobenzene layer in section with 25% H_2O. I) 80% hexane, II) 70% hexane, III) 60% hexane, IV) 50% hexane.

of a given section (Figs. 3-7), we select the known indexes of refraction and find the percentage content of aniline ($x_1x_2x_3$) in the mixtures which belong to the same nodal section of the triangle of the three liquid phases. Points $x_1x_2x_3$ are placed on the horizontal sections I, II, and III of the composition triangle and thus the sections of the nodal triangle are obtained.

Tables 1-3 contain the data for the construction of sections of nodal triangles which are shown in Figs. 8-10.

In order to locate the boundaries of the region of existence of three liquid phases in each horizontal section we made use of the Alekseev polythermic method [3]. We do not cite the study of the edges of the tetrahedron of water-aniline-nitrobenzene, water-aniline-hexane and water-hexane-nitrobenzene. The study of the edge of aniline-nitrobenzene-hexane was reported in our previous paper [1].

TABLE 4

Index of refraction corresponding to the nodal section of the triangle	Weight % of aniline for sections with:		
	75% H_2O	50% H_2O	25% H_2O
1.3875	83.00	72.00	67.30
1.3900	72.00	60.00	57.50
1.3950	45.00	42.00	40.00
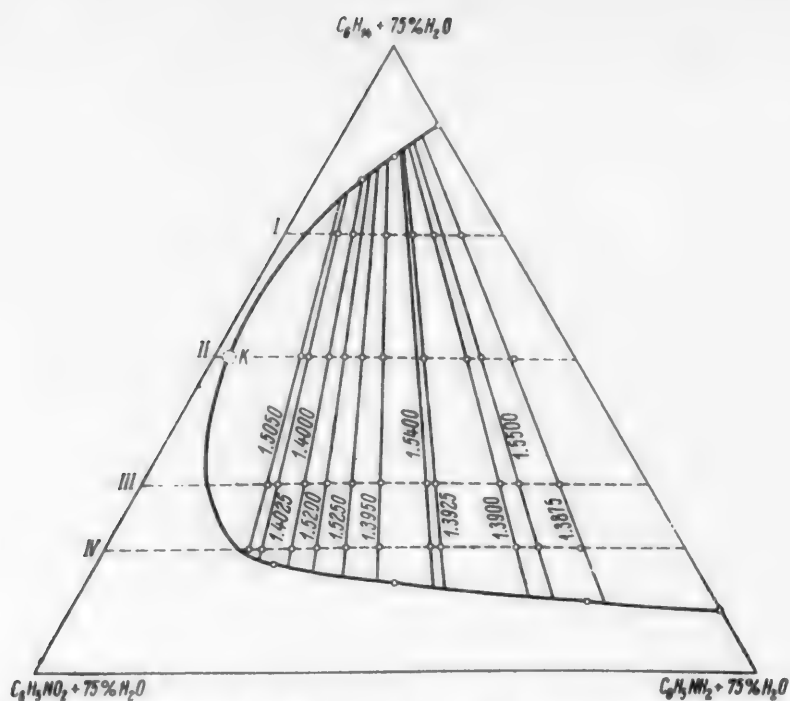
Fig. 8. Section with 75% H_2O.
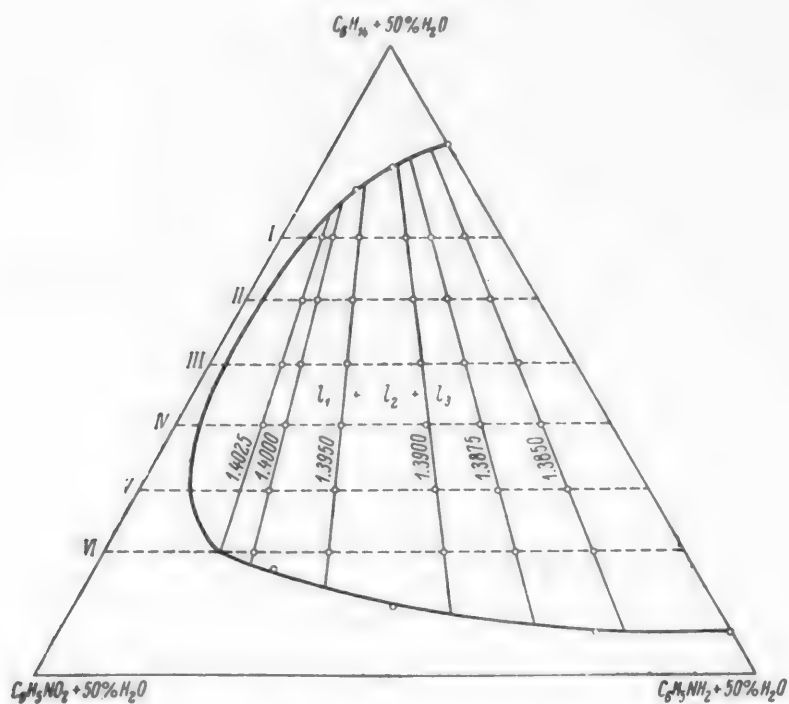
Fig. 9. Section with 50% H_2O.
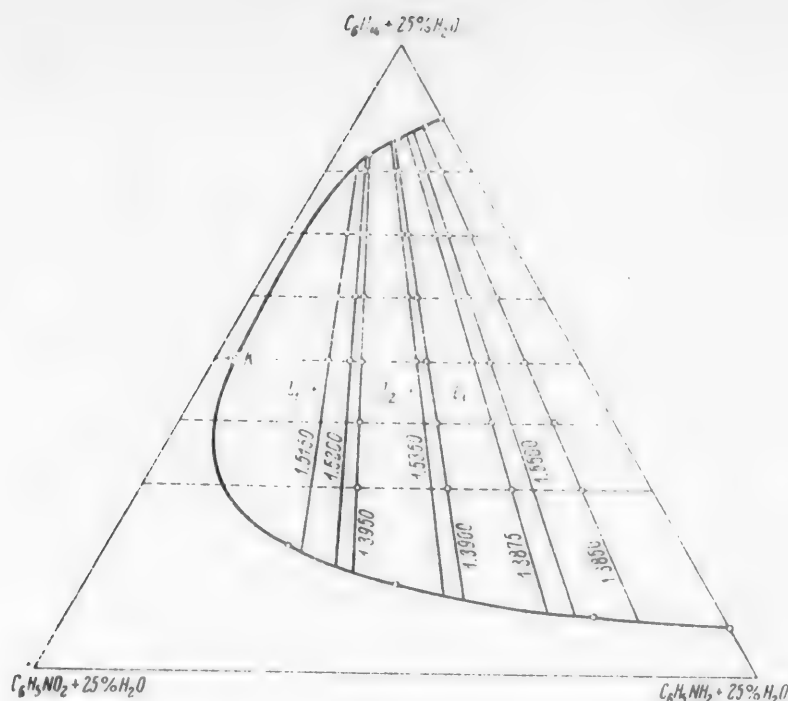
Fig. 10. Section with 25% H_2O.
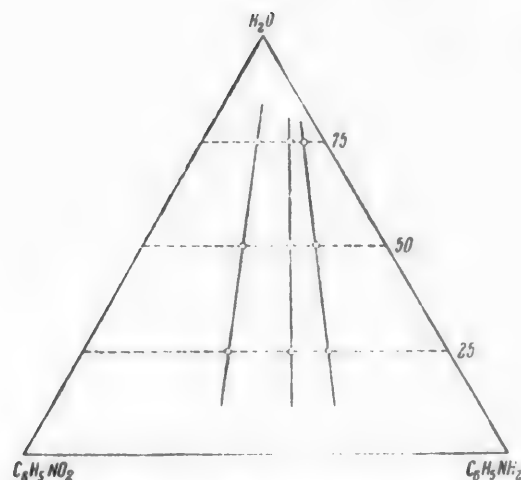
Fig. 11. Clinographic projection of ends of nodal sections of triangles of three liquid phases.

DISCUSSION OF RESULTS

All the horizontal sections show a similar picture of the region of existence of three liquid phases. The nodal triangles have the same direction — right in respect to the secant drawn through the vertex to the nitrobenzene-aniline side. During the preparation of the mixtures we discovered a critical opalescence for compositions with 1.87% water, 37.50% hexane and 35.63% nitrobenzene (section corresponding to 25% water) and 0.5% aniline, 12.0% nitrobenzene and 12.5% hexane (section corresponding to 75% water). The existence of critical opalescence permits us to judge the location of the critical node. This is directed toward the edge of n-hexane-nitrobenzene-water indicating the tendency of formation of three liquid phases in this system. Actually, three liquid phases were discovered at 15°.

By clinographical projection of the ends of the nodal sections of the triangles which correspond to the known indexes of refraction of the nitrobenzene layer for each section of the side edge water-nitrobenzene-aniline we obtain points which lie on the same straight line, this fact indicating that these projections belong to the plane of one triangle. The data for the construction of the projection picture are given in Table 4, while the clinographic projection is shown in Fig. 11.

It is evident from Fig. 11 that these projections have the same direction, specifically, left, which fact coincides with the direction of the nodes in the system of water-nitrobenzene-aniline. The binodal curves meet at the side of water-aniline; the critical point is located to the right of it in the imaginary area and because of this the nodes must have the left directivity.

SUMMARY

1. The four-component system was studied as to equilibrium of the three liquid phases.

2. The possibility of application of the section method to the study of equilibrium of three liquid phases in a four-component system was shown.

3. It was established that the rule about the direction of nodes maintains its force in the four-component system as well, in the matter of disposition of intersections of nodal triangles by sections parallel to the base of the tetrahedron.

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*Original Russian pagination. See C.B. Translation.

CONCERNING COMPOUNDS OF LUTEOPHOSPHOTUNGSTIC ACID WITH UREA AND GLYCINE

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Compounds of luteophosphotungstic acid $H_{12}[P_2O_2(W_2O_7)_9] \cdot xH_2O$ (we shall denote it by l.p.w. below) with organic nitrogenous bases which have been described in the literature are quite few in number. Thus, Rosenheim and Jaenicke [1] prepared a trisubstituted salt of guanidine with the empirical composition $3(CN_3H_6)_2O \cdot P_2O_5 \cdot 18WO_3 \cdot 10H_2O$, which had the appearance of small yellow prisms. A very sparingly soluble guanidine salt was prepared by the action of five moles of sodium hydroxide and excess guanidine chloride on the free acid, this salt separating from the solution in the form of small plate-like crystalline aggregates with empirical composition $5(CN_3N_6)_2O \cdot P_2O_5 \cdot 18WO_3 \cdot 18H_2O$. The l.p.w. acid differs materially in this respect from phosphotungstic acid of the saturated series $H_7[P(W_2O_7)_6 \cdot xH_2O]$ for which an extensive literature exists, as a precipitant for organic bases, amino acids and others, this literature being partially cited in paper [2].

We set for our goal a study of the compounds of l.p.w. acid with urea and glycine. These compounds have not been described in the literature as yet. A similar compound of phosphotungstic acid $H_7[P(W_2O_7)_6] \cdot xH_2O$ is moderately soluble in water and is precipitated in case the urea concentration in solution exceeds 2% [3].

As is known, urea forms salts with strong acids, reacting with one equivalent of the acid. Its difficultly soluble salts with composition $CO(NH_2)_2 \cdot HNO_3$, $2CO(NH_2)_2 \cdot H_2C_2O_4$, etc. are known. These salts are decomposed by water according to some reports [4].

EXPERIMENTAL

Preparation of Salts of Urea with l.p.w. Acid

The urea used by us for this work had m.p. 132-133°. The l.p.w. acid was prepared by us by Wu's method [5]: 200 g of $Na_2WO_4 \cdot 2H_2O$ was dissolved in one liter of water, 280 g of 85% H_3PO_4 was added to the solution and the mixture was refluxed for eight hours. Ammonium l.p.w. was precipitated from the solution after cooling by addition of 200 g of finely powdered ammonium chloride. The resulting ammonium l.p.w. was dissolved in 600 ml of water and was reprecipitated twice by salting out with 200 g of ammonium chloride, after which it was once more dissolved in water and was crystallized finally by being heated on a water bath. Only the β-form of ammonium l.p.w., having the composition $(NH_4)_6H_6[P_2O_2(W_2O_7)_9] \cdot 11H_2O$ was used for the preparation of the acid.

The etherate of l.p.w. acid, which crystallized at room temperature, was isolated from the hydrochloric acid solution of the ammonium salt. The resulting acid had the following composition (in %): residue after heating – 85.33, P_2O_5 – 2.81, NH_3 – 0.16, H_2O – 14.51.

Recrystallization from water failed to lower the content of NH_3 in the specimen; after the recrystallization we obtained a specimen with the composition (in %): residue after heating – 85.40, P_2O_5 – 2.88, NH_3 – 0.19, H_2O – 14.41. It is possible to consider, starting with these data, that the acid has the empirical composition $P_2O_5 \cdot 18WO_3 \cdot 40H_2O$ or the coordination formula $H_{12}[P_2O_2(W_2O_7)_9] \cdot 34H_2O$.

Later, in the analysis of compounds of urea and glycine with l.p.w. acid we introduced the corrections for ammonia contained in the acid.

A 2.47M solution of urea was added to the aqueous 0.1M solution of l.p.w. acid in amounts needed to prepare di-, tetra, hexa-, octa- and dodeca-substituted salts of urea. The solution remained yellow after the mixing of solutions of urea and l.p.w. acid, and only after several days was there noted in the solution, treated with eight and twelve equivalents of urea, a weak blue color owing to the partial reduction of the W^{VI} anion. The crystallization was run in desiccators over sulfuric acid and proceeded rapidly. Aggregates of large – length up to several millimeters – crystals with pale yellow color formed on the dish walls. The specimens were analyzed after having been isolated, washed and dried at room temperature and ground in an agate mortar. The residue after heating, phosphorus and nitrogen were determined in the air-dry samples. Phosphorus was precipitated as $MgNH_4PO_4$ after destruction of the complex with sodium hydroxide by boiling and was re-precipitated as directed by Wu. The solution being analyzed was first cooled with ice, prior to precipitation of the phosphate ion. The isolation of the $MgNH_4PO_4$ precipitate was done on the following day. Nitrogen was determined by Kjeldahl method and was calculated on the basis of urea. The combustion was completed over several hours. The control of the resulting data on the content of urea in the salts was done by the method of A. P. Borodin [6], which is based on oxidation of urea with hypobromite according to the equation:

$$CO(NH_2)_2 + 3NaBrO = N_2 + CO_2 + 3NaBr + 2H_2O.$$
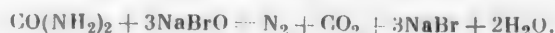
The content of urea in the salts was calculated from the volume of evolved nitrogen. For running the analysis we dissolved a 0.6-1.0 g sample of the specimen in 25 ml of water and an aliquot of 6-7 ml was taken from the resulting solution for the analysis. The results of the analyses are given in Table 1.

TABLE 1

Results of Analysis of Salts of Urea with l.p.w Acid (in %)

Calculated degree of substitution	Found *					H_2O by difference	Ratio $P_2O_5 : WO_3$
	P_2O	residue after heating	WO_3 by difference	by Kjeldahl method	by Borodin method		
2	2.98	89.30	86.32	2.97	2.67	7.73	1 : 17.7
4	2.83	88.26	85.43	5.30	4.96	6.44	1 : 18.5
6	3.06	88.62	85.56	7.19	7.08	4.19	1 : 17.2
8	—	88.48	—	9.68	—	3.84	—
12	2.86	84.21	81.35	13.79	13.25	2.01	1 : 17.5

*Mean values obtained in analyses of air-dried samples.

TABLE 2

Composition of Salts of Urea with l.p.w. Acid

No. of urea equiv. introduced	Empirical formula of the resulting salts
2	$2(NH_2)_2CO \cdot P_2O_5 \cdot 18WO_3 \cdot 21H_2O$
4	$4(NH_2)_2CO \cdot P_2O_5 \cdot 18WO_3 \cdot 18H_2O$
6	$6(NH_2)_2CO \cdot P_2O_5 \cdot 18WO_3 \cdot 11H_2O$
8	$8(NH_2)_2CO \cdot P_2O_5 \cdot 18WO_3 \cdot 10H_2O$
12	$11.5(NH_2)_2CO \cdot P_2O_5 \cdot 18WO_3 \cdot 6H_2O$

The empirical composition of the resulting salts was calculated from the data in Table 1; the data are given in Table 2.
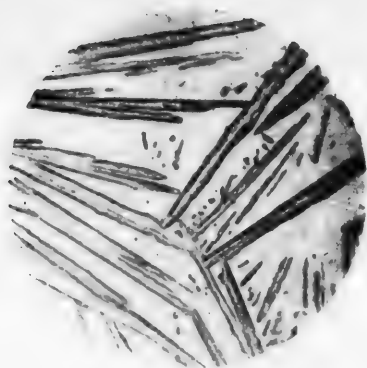
Fig. 1. Crystals of urea.

A microscopic examination of the crystals of l.p.w. urea showed that they differ in their form from crystals of urea or of l.p.w. acid (see Figs. 1-5). The resulting urea salts of l.p.w. acid have rather good solubility in water.

The values of pH (with quinhydrone electrode) of the 0.01M solutions of the resulting salts were determined and compared with the corresponding pH values of solutions of urea and free l.p.w. acid (Table 5). These measurements indicate that introduction of urea into a solution of l.p.w. acid raises the pH only very slightly. This distinguishes the salts formed by urea from the highly substituted sodium and potassium salts of heteropoly acids described in the literature [7]; at the same time the amount of hydrate water content of all these salts is considerably smaller than that of the original l.p.w. acid. Also, the amount of hydrate water drops with an increase of the number of equivalents of urea in the salt; the salt containing 11.5 equivalents of urea contains practically no hydrate water. The insignificant shift of pH in solutions of these salts after addition of urea permits us to regard these salts as salt-like products of addition of urea to l.p.w. acid with the following formulas:

$$H_{12}[P_2O_2(W_2O_7)_9] \cdot 2(NH_2)_2CO \cdot 15H_2O$$
$$H_{12}[P_2O_2(W_2O_7)_9] \cdot 4(NH_2)_2CO \cdot 12H_2O$$
$$H_{12}[P_2O_2(W_2O_7)_9] \cdot 6(NH_2)_2CO \cdot 5H_2O$$
$$H_{12}[P_2O_2(W_2O_7)_9] \cdot 8(NH_2)_2CO \cdot 4H_2O$$
$$H_{12}[P_2O_2(W_2O_7)_9] \cdot 11.5(NH_2)_2CO$$
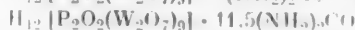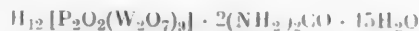
Let us note that a rapid introduction of ten equivalents of urea into 0.2M solution of l.p.w. acid led to the formation of a compound having the following composition (in %): residue after heating — 78.72, NH_3 — 10.87, urea — 19.78, which corresponded to the salt-like addition product of 18 equivalents of urea to l.p.w. acid. Evidently part of the acidic hydrogen ions in this compound is replaced by urea since this salt contains less water than does the free l.p.w. acid; the remaining urea molecules react with the heteropoly acid, forming addition products.
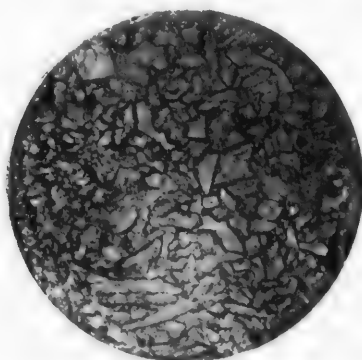
Fig. 2. Salt with 2 equivalents of urea.

Fig. 3. Salt with 4 equivalents of urea.

It is also possible to suppose that these compounds are salts of l.p.w. acid with different degrees of substitution, subjected to hydrolysis in the aqueous solution. A complete understanding of the nature of these compounds requires some new and systematic studies of salts of urea with various acids.

Preparation of Salts of Glycine with l.p.w. Acid

As is known, glycine is an ampholyte; it gives salts with acids and bases; compounds with the following composition have been described:

$$2 \text{ Gly} \cdot \text{HCl}, \ 2\text{Gly} \cdot \text{H}_2\text{SO}_4, \ \text{Gly}_3\text{H}_4[\text{P}(\text{W}_2\text{O}_7)_6] \cdot 6\text{H}_2\text{O}[8].$$

Van Slyke [9] studied the solubility of the phosphotungstic salt of glycine in the presence of various concentrations of HCl (from 0.25 to 3N) at 22° and discovered that beginning with 2N solutions of hydrochloric acid and higher, the solubility of $\text{Gly}_3\text{H}_4[\text{P}(\text{W}_2\text{O}_7)_6] \cdot x\text{H}_2\text{O}$ decreases.

Fig. 4. Salt with 6 equivalents of urea.

Fig. 5. Salt with 8 equivalents of urea.

For preparation of the salts we used a specimen of l.p.w. acid, whose analysis was given above, and glycine with decomposition point 233°. The salts of l.p.w. acid with glycine were prepared by mixing the calculated amounts of aqueous 2.5M solution of glycine and 0.19M solution of l.p.w. acid. The solutions remained yellow after mixing but after several days the solutions to which ten or more equivalents of glycine had been added, became blue (reduction of W^{VI} anion). Solutions containing 3.6 and 8 equivalents of glycine yielded yellow crystals on the walls and the bottom of the porcelain dish and became coated with a crystalline film on top. Solutions containing 10, 12 and 18 equivalents of glycine turned into a sirupy blue mass on standing, this mass solidifying to a glass on top. Later the entire liquid under this layer changed into a glassy mass. It was discovered after several weeks that the lower layer of the specimen into which 12 equivalents of glycine had been introduced consists of tetragonal crystals, with dimensions of 4-6 mm, having the form of plates composed of radially disposed needles. The crystals were separated mechanically from the upper layer and were washed. Evidently a process of glazing of the viscous masses of the salt occurs during the several weeks of standing.

Later, in the preparation of highly substituted salts,the viscous blued solutions, containing the necessary amount of glycine, were subjected to cooling to $-2°$ even before the appearance of the film on their surfaces. Crystals which appeared in the cooled solutions had the appearance of six or four-sided almost colorless plates which floated on the surface and gradually increased in size. The crystals were left at room temperature after having been separated by decantation. They dissolved in their own water of crystallization and changed into a viscous liquid which was left at room temperature until it hardened. The glassy mass formed in the solutions was subjected to analysis.

The results of the analyses are given in Table 3. Samples of the specimens were first dried at 100-110° since they remained damp for a long time during air-drying. The phosphorus determination was done by the method described above. The decomposition of the samples in sulfuric acid for the ammonia determination required several tens of hours during the work with derivatives of glycine. The solution became transparent toward the end of the decomposition and the WO_3 precipitate became yellow. An attempt to accelerate the decomposition by addition of several drops of 30% hydrogen peroxide led to a partial loss of nitrogen.

There are indications in the literature about the need for a long decomposition for the nitrogen determination in salts of isopoly- and heteropoly compounds with amino acids. The samples could not lose all the water of crystallization as the result of drying at 100-110°; for this reason the degree of subsutution (x) in this case was determined not by comparison of the experimental data with the theoretical ones, but by means of the formula:

$$x = \frac{M_{\text{P}_2\text{O}_5} \cdot 18\text{WO}_3 \cdot \% \ \text{CH}_2\text{NH}_2\text{COOH}}{M_{\text{CH}_2\text{NH}_2\text{COOH}} \cdot \% \ \text{residue after heating in a furnace}}$$

The composition of the substances prepared with glycine were calculated on the basis of the data in Table 3.

In the specimen prepared after the preliminary cooling and decantating the resulting crystals have a low content of glycine (Table 4).

TABLE 3

Composition of Salts of Glycine with l.p.w. Acid (in %)

| Conditions of synthesis | No. of equiv. of glycine added | Found [*] | | | | | Ratio P_2O_5: WO_3 |
		P_2O_5	incombustible residue	WO_3 by difference	CH_2NH_2COOH	H_2O by difference	
Crystallization at room temperature	3	3.05	91.66	88.63	5.58	2.36	1 : 18
	6	3.02	88.44	85.42	10.03	1.53	1 : 17.4
	8	2.82	87.47	84.65	11.63	0.90	1 : 18.4
Same – crystals from crystallized glass	12	2.66	81.66	79.00	16.87	1.47	1 : 18.2
Crystallization at –2°	10	2.80	87.95	85.15	10.77	1.28	1 : 18.8
	12	2.77	82.62	79.85	15.79	1.59	1 : 17.7
Excess of glycine		2.44	74.15	71.71	23.24	2.61	1 : 18.1

[*]Mean values from two-three determinations. Samples dried at 100-110° were subjected to the analysis.

The form of the crystals of glycine salts differs from that of the crystals of the starting material (Figs. 6-9).

Compounds of glycine with l.p.w. acid contain considerably less water of hydration than does the original heteropoly acid. The smallest amount of water — practically a deficiency of salt-forming water – is found among the glycine salts prepared with eight and ten equivalents. Further studies in the areas of synthesis, analysis and physicochemical measurements should solve this problem.

TABLE 4

Composition of Salts of Glycine with l.p.w. Acid

No. of glycine equiv. introduced	Empirical formulas of preparations obtained
3	$3CH_2NH_2COOH \cdot P_2O_5 \cdot 18WO_3 \cdot 7H_2O$
6	$6CH_2NH_2COOH \cdot P_2O_5 \cdot 18WO_3 \cdot 4H_2O$
8	$8CH_2NH_2COOH \cdot P_2O_5 \cdot 18WO_3 \cdot 2H_2O$
10	$7CH_2NH_2COOH \cdot P_2O_5 \cdot 18WO_3 \cdot 3H_2O$
12	$12CH_2NH_2COOH \cdot P_2O_5 \cdot 18WO_3 \cdot 4H_2O$
12	$11.5CH_2NH_3COOH \cdot P_2O_5 \cdot 18WO_3 \cdot 4H_2O$
Excess of glycine	$18CH_2NH_2COOH \cdot P_2O_5 \cdot 18WO_3 \cdot 8H_2O$

The results of pH measurements of the 0.01 M aqueous solutions of salts of glycine with l.p.w acid are given in Table 5. These data show that an increase of the glycine content in the specimens shifts the pH of the solutions more energetically to the alkaline side than is seen among the urea salts.

Determinations of the pH of aqueous solutions of salts of glycine with l.p.w. acid indicate a partial neutralization of the hydrogen ions of the heteropoly acid and, thus, a formation of acid salts, in the formation

of which the basic function of glycine is manifested. These salts may be given the specimen formula:

$$H_{12-x}(\overset{+}{N}H_3CH_2COOH) \cdot x[P_2O_2(W_2O_7)_9] \cdot x H_2O.$$
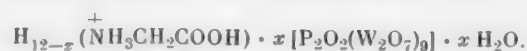
On the other hand, for salts prepared by the action of 10, 12 or 18 equivalents on the l.p.w. acid, we discovered the formation of a very viscous glass-like solution. A similar phenomenon was observed among the glycine complexes of platinum [10] and for analogous complexes of chromium [11]. The formation of viscous

Fig. 6. Glycine crystals.
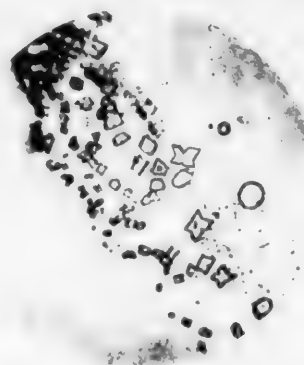
Fig. 7. Salt with 4 equivalents of glycine.

solutions of glass-like masses, and then the formation of a salt with 18 equivalents, must be explained by polymerization of glycine molecules at their hydrogen bonds which arise between the carboxyls of their molecules; in addition, the hydrogen bonds may easily form in solution at the hydrogen atoms of the water of hydration of the heteropoly acid and the oxygen in the glycine carboxyl. It seems premature to suggest the structural formulas of the compounds prepared by us at this time.

TABLE 5

Values of pH of Salts of Urea and Glycine With l. p. w. Acid
(0.01 M solution)

Compound	pH
$H_{12}[P_2O_2(W_2O_7)_9] \cdot xH_2O$	1.36
CH_2NH_2COOH	5.46
$CO(NH_2)_2$	5.63
$2(NH_2)_2CO \cdot P_2O_5 \cdot 18WO_3 \cdot xH_2O$	1.72
$4(NH_2)_2CO \cdot P_2O_5 \cdot 18WO_3 \cdot xH_2O$	1.74
$6(NH_2)_2CO \cdot P_2O_5 \cdot 18WO_3 \cdot xH_2O$	1.77
$12(NH_2)_2CO \cdot P_2O_5 \cdot 18WO_3 \cdot xH_2O$	1.81
$3(CH_2NH_2COOH) \cdot P_2O_5 \cdot 18WO_3 \cdot xH_2O$	1.89
$6(CH_2NH_2COOH) \cdot P_2O_5 \cdot 18WO_3 \cdot xH_2O$	2.32
$7(CH_2NH_2COOH) \cdot P_2O_5 \cdot 18WO_3 \cdot xH_2O$	2.39
$11.5(CH_2NH_2COOH) \cdot P_2O_5 \cdot 18WO_3 \cdot xH_2O$	2.69

We shall note that the l.p.w compounds of glycine are very readily soluble in water.

Addition of hydrochloric acid to concentrated solutions of glycine salt of l.p.w. acid causes the precipitation of the latter, evidently by salting out of the compounds by a strong electrolyte.
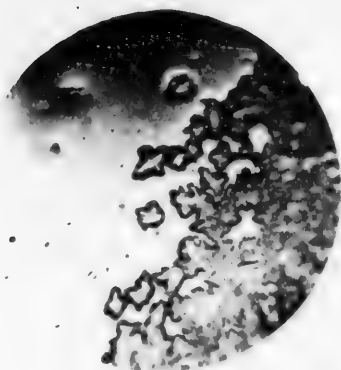
Fig. 8. Salt with 7 equivalents of glycine.
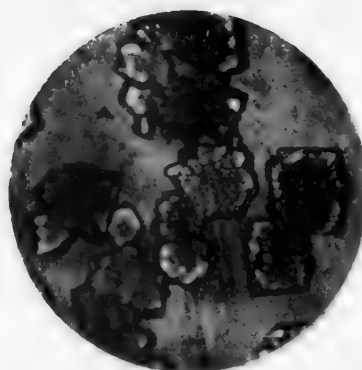
Fig. 9. Salt with 6 equivalents of glycine.

SUMMARY

1. Salts of luteophosphotungstic acid with urea were prepared and the values of pH of the solutions of these compounds were determined. It is possible to regard these salts, on the basis of these data, as being the addition products of urea to luteophosphotungstic acid.

2. Crystalline salts of luteophosphotungstic acid with glycine were prepared. The pH of solutions of these compounds were measured. On the basis of the acidic properties of these compounds, we may report the formation of glycine salts with manifestation of the basic properties of glycine; the glycine molecules in the highly substituted salts are partly polymerized at their hydrogen bonds.

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A STUDY IN THE FIELD OF VAPOR PHASE HYDRATION OF ACETYLENE AND ITS DERIVATIVES

IV. ADDITION OF ETHYL AND BUTYL ALCOHOLS TO VINYLACETYLENE UNDER THE INFLUENCE OF SOLID CATALYSTS

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The reaction of vinylacetylene with alcohols is of considerable interest since, depending on the selection of the catalyst and the reaction conditions, it leads to formation of different substances. Thus, according to [1], the addition of methanol to vinylacetylene in the presence of sodium methoxide at 100° leads to formation of 4-methoxy-1-butyne. 2,2,4-Trimethoxybutane was prepared by the reaction of vinylacetylene with methyl alcohol in the presence of mercuric oxide and boron trifluoride [2]. The addition of alcohols to vinylacetylene under pressure with potassium hydroxide catalyst [3] proceeds with formation of allenic ethers in the case of methyl alcohol; other alcohols yield under the same conditions the β-ethers with conjugated double bonds. According to [4] the addition of alcohols to vinylacetylene homologs also leads to formation of dienic ethers. However, the reaction of substituted acetylenes with methanol under the influence of mercuric oxide and boron trifluoride leads to formation of ketals [5].

In has been shown by one of us [6] that ethyl and butyl alcohols add in vapor phase to acetylene at 325° under the influence of zinc oxide as the catalyst and form vinyl ethyl ether in the first case, or vinyl butyl ether in the second case. By drawing an analogy between the addition of these alcohols to acetylene over a solid catalyst and the addition of water to acetylene under the same conditions, the authors expressed the supposition that the first product of addition of water to acetylene is vinyl alcohol (analog of vinyl ether), which then isomerizes to acetaldehyde. An attempt was made in the present work to clarify the possibility of addition of alcohols to vinylacetylene under the influence of solid catalysts, in an anology to the addition of water to it [7]. Zinc oxide was again selected as the catalyst.

It was established as the result of the study of the reaction of vinylacetylene with ethyl and butyl alcohols that two molecules of butyl alcohol add to the hydrocarbon at its acetylenic bond, with formation of a ketal.

$$\text{CH}_2\!=\!\text{CH}\!-\!\text{C}\!\equiv\!\text{CH} + 2\text{C}_4\text{H}_9\text{OH} \rightarrow \text{CH}_2\!=\!\text{CH}\!-\!\overset{\displaystyle \text{OC}_4\text{H}_9}{\underset{\displaystyle \text{OC}_4\text{H}_9}{\text{C}}}\!-\!\text{CH}_3$$
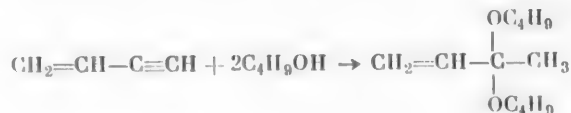
The reaction products of vinylacetylene and ethyl alcohol were isolated in insignificant amounts, probably owing to their poor stability under the reaction conditions.

EXPERIMENTAL

The catalyst — zinc oxide, mark M-1 (GOST 202-41) — was pressed into tablets with a laboratory hydraulic press. The tablets were broken into 3-4 mm pieces and were charged in this form into an oven. Ethyl alcohol — anhydrous — was refluxed over CaO and distilled, b.p. 78-78.3°, d^{20}_4 0.7898, n^{20}D 1.3611. Butyl

alcohol — mark Chemically Pure — was dried with calcium oxide and subjected to distillation; b.p. 116.5-117°, d_4^{20} 0.8095, n_D^{20} 1.3996. Vinylacetylene — "rectificate" with 99.5% assay; b.p. +5°.

The experiments were run in a laboratory catalytic oven [7] at 250° and 300°. The ratio of vinylacetylene to alcohol was 1 : 3 moles. Duration of a run was three hours. The resulting condensate was heated on a water bath to 40° in order to remove the dissolved vinylacetylene from the liquid reaction products.

The condensate obtained from several experiments with ethyl alcohol (space velocity of vinylacetylene — 30 liters/liter of catalyst per hour) was subjected to distillation, 262.6 g being used. Besides the main bulk of ethyl alcohol, diethyl ether and acetaldehyde, we isolated a small amount of 3,3-diethoxy-1-butene, b.p. 69° (100 mm), n_D^{20} 1.4068.

Found %: C 66.98; H 11.34. M 139.5. $C_8H_{16}O_2$. Calculated %: C 66.68; H 11.19. M 144. Literature data [8]: b.p. 69° (100 mm), n_D^{20} 1.4062.

The condensate obtained from several experiments with butyl alcohol (space velocity of vinylacetylene — 50 liters/liter of catalyst per hour) was also subjected to distillation in the amount of 384 g. Besides the unreacted butyl alcohol and butyraldehyde, we isolated 3,3-dibutoxy-1-butene in the yield of about 20% based on the reacted vinylacetylene.

B.p. 78-80° (8 mm), d_4^{20} 0.8440, n_D^{20} 1.4248. Found %: C 72.35; H 12.76. M 192.5. $C_{12}H_{24}O_2$. Calculated %: C 71.91; H 12.09. M 200. Literature data [8]: B.p. 78-80° (8 mm), d_4^{20} 0.8497, n_D^{20} 1.4238.

Methyl vinyl ketone (b.p. 80°, n_D^{20} 1.4078; m.p. of semicarbazone 140-41°) and butyl alcohol (b.p. 116.5-117°, d_4^{20} 0.8087, n_D^{20} 1.3998) were found among the hydrolysis products of 3,3-dibutoxy-1-butene under the influence of 4% sulfuric acid.

SUMMARY

The catalytic reaction of vinylacetylene with ethyl and butyl alcohols over zinc oxide was studied at 300°. The possibility of formation under these conditions of unsaturated ketals in yields up to 20% was demonstrated.

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SYNTHESIS AND TRANSFORMATIONS OF ORGANOSILICON VINYL ETHERS

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The methods of synthesis and the properties of vinyl ethers have been studied sufficiently well [1]. However, the chemistry of organosilicon vinyl ethers has not been illuminated at all in the chemical literature. Vinyl ethers of γ-silicon-containing alcohols, prepared by the Favorskii–Shostakovskii method, are described by us in the present paper. At the same time, we should call attention to the fact that numerous attempts made to prepare the vinyl ethers of silanols, α- and β-silicon-containing alcohols failed, when the above method was used.

Vinylation of trialkyl- and dialkylarylsilanols, both in the presence of alkalies (NaOH and KOH) as well as in the presence of sodium silanolates and potassium silanolates, usually led to formation of hexaalkyl (aryl)-disiloxanes.

$$2R_3SiOH + CH\equiv CH \rightarrow R_3SiOSiR_3 + H_2O$$

Vinylation of α-silicon-containing alcohols in the presence of potassium hydroxide and potassium alcoholates of these alcohols led to the formation of ethers.

$$2R_3SiCH_2OH + CH\equiv CH \rightarrow R_3SiCH_2-O-CH_2SiR_3 + H_2O$$
$$R = alkyl$$
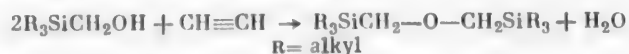
Evidently, the rate of reaction of dehydration of silanols and γ-silicon-containing alcohols exceeds the reaction rate of vinylation in the preparation of vinyl ethers of these compounds by this method and suppresses the latter.

Hexaalkyl(aryl) disiloxanes, resins and water were the main reaction products in an attempt to prepare β-silicon-containing vinyl ethers by an analogous route.

$$2R_3SiCH_2CHOHCH_3 + CH\equiv CH \rightarrow R_3SiOSiR_3 + H_2O + resin$$

Vinylation of γ-silicon-containing alcohols was undertaken in this connection. As the result of these studies we succeeded in showing the applicability, in principle, of the Favorskii–Shostakovskii reaction to the preparation of γ-silicon-containing vinyl ethers [2], using the example of the vinyl ether of γ-hydroxypropyl-trimethylsilane.

$$(CH_3)_3SiCH_2CH_2CH_2OH + CH\equiv CH \rightarrow (CH_3)_3SiCH_2CH_2CH_2OCH\equiv CH_2$$

The vinylation of primary γ-silicon-containing alcohols was studied for the clarification of the optimum conditions of synthesis of γ-silicon-containing vinyl ethers by this method, using different conditions, and the role of the catalyst, acetylene pressure, reaction temperature and solvents was established [3-5].

A study of the vinylation process of the indicated alcohols under the influence of potassium hydroxide showed that the reaction proceeds very slowly under these conditions (at 170-180°) and is accompanied by much resin formation of the reaction mixture, which leads to low yields of the final products. The maximum yields of γ-silicon-containing vinyl ethers reached 35-38% under these conditions. The presence of water in the reaction medium has a negative effect.

Since the catalytic action of potassium hydroxide turned out to be poorly effective, this was replaced by metallic potassium, i.e., the potassium alcoholates of the starting alcohols were used as the catalysts. In this case the vinylation reaction proceeded under milder conditions (150-160°) and with less tar formation in the reaction mixture. The yields of γ-silicon-containing vinyl ethers reached 65-68%, i.e., were twice as high as in the case of application of potassium hydroxide. As to the influence of water, it turned out that its presence hinders the reaction.

Thus, behavior of primary γ-silicon-containing alcohols in this reaction indicates that the vinylation of them in the presence of potassium hydroxide proceeds by the Favorskii-Shostakovskii scheme [1], through a stage of formation of potassium alcoholate.

$$R_3SiCH_2CH_2CH_2OH + KOH \rightarrow R_3SiCH_2CH_2CH_2OK + H_2O$$
$$R = \text{ organic radical}$$
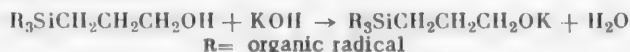
The drop of the yields of vinyl ethers and the abundant resin formation during the vinylation in the presence of potassium hydroxide are evidently connected with the difficulty of formation of the alcoholates. Then, the addition of the alcoholate to acetylene takes place. The above vinylation scheme is well confirmed by the fact that the use of one of the intermediate products, specifically potassium alcoholate, as the catalyst sharply raises the yield of γ-silicon-containing vinyl ethers, while the presence of water hinders the vinylation.

Later we attempted to extend the Favorskii-Shostakovskii reaction to the tertiary γ-silicon-containing alcohols of the acetylenic, the ethylenic and the saturated series. However, all attempts to prepare vinyl ethers based on tertiary γ-silicon-containing alcohols turned out to be failures. Vinylation of tertiary γ-silicon-containing alcohols of the saturated series in general failed to go, the absorption of acetylene was not observed and only an insignificant tarring of the initial alcohol occurred. The vinylation reaction of tertiary γ-silicon-containing alcohols of the ethylenic and the acetylenic series was accompanied by cleavage of the Si—C bond, according to the scheme below, both under the influence of potassium hydroxide and under the influence of their alcoholates:

$$R_3SiCH=CH-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-OH + CH\equiv CH \rightarrow R_3SiOSiR_3 + \text{ resin}$$

$$R_3SiC\equiv C-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-OH + CH\equiv CH \rightarrow R_3SiOSiR_3 + \text{ resin}$$

$$R = CH_3 \text{ and } C_2H_5$$
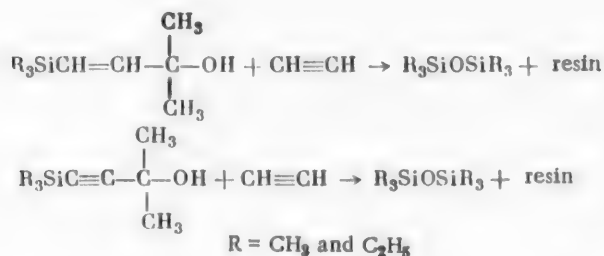
The behavior of primary and tertiary γ-silicon-containing alcohols in the vinylation reaction resembles the properties of their organic analogs but, despite this, they display some difference from the latter. Primary γ-silicon-containing alcohols are vinylated with considerable difficulty in the presence of potassium hydroxide. The use of potassium alcoholate is necessary for their vinylation, while their organic analogs enter this reaction most readily even in the presence of potassium hydroxide. While tertiary alcohols are still vinylated in the presence of potassium alcoholates, the tertiary γ-silicon-containing alcohols do not enter the vinylation reaction under these conditions.

γ-Silicon-containing vinyl ethers are colorless, mobile volatile liquids which have a pleasant ethereal odor, are insoluble in water but easily soluble in organic solvents. Boiling points, densities and indexes of refraction of γ-silicon-containing vinyl ethers rise with increased molecular weight of the ether. These are unassociated compounds since they boil at lower temperatures than do the corresponding alcohols, although their molecular weight is higher than that of the corresponding original alcohols. The γ-silicon-containing vinyl ethers enter almost all the chemical reactions which are characteristic of organic vinyl ethers; however, despite this, they differ materially from the latter. It is characteristic of the γ-silicon-containing vinyl ethers to react by both the ionic and the free-radical mechanisms. The γ-silicon-containing vinyl ethers have a number of general symptoms in the reactions which proceed by the ionic mechanism, while having at the same time some differences in comparison with their organic analogs. The generality consists of the fact that the addition reactions of water, alcohols, silanols, organic acids and other compounds are catalyzed by acidic substances

(HCl, FeCl₃, etc.) both for γ-silicon-containing vinyl ethers and for the vinyl alkyl ethers. The addition products are formed in accord with the Markovnikov rule, i.e., the addition reactions of various substances to γ-silicon-containing vinyl ethers under the influence of ionic catalysts proceed by the ionic mechanism through the stage of formation of oxonium compounds, and the latter break down later with formation of the carbonium ions. These reactions proceed more slowly and require higher temperatures and longer time intervals for their completion than the γ-silicon-containing vinyl ethers. At the same time, the resulting addition products are more stable, as it will be shown during the examination of each reaction separately. This difference in respect to the polymerization reaction is displayed particularly clearly.

We failed to prepare polymers from γ-silicon-containing vinyl ethers under the influence of free radical catalysts, while vinyl alkyl ethers are polymerized in the presence of the latter substances, although poorly. At the same time, it is still impossible to assert categorically on the basis of our experiments that the free radical polymerization of γ-silicon-containing vinyl ethers is impossible, especially since they do form copolymers with methyl methacrylate under the influence of benzoyl peroxide and azoisobutyronitrile. Evidently, the γ-silicon-containing vinyl ethers react with free radicals more difficultly if the free valence of the latter is that of oxygen, than in the case in which the free valence is that of a carbon atom.

Thus, the presence of the silicon atom in the γ-position in vinyl ethers places its imprint on the behavior of these ethers in various chemical transformations. In connection with this fact that the indicated peculiarities of chemical properties of the γ-silicon-containing vinyl ethers have a general significance in the chemistry of organosilicon compounds, let us examine each of their reactions separately and let us compare the reactivities of these compounds with those of vinyl alkyl ethers.

One characteristic of vinyl ethers is their ability to be hydrolyzed in acidic medium, with the rate of the hydrolysis reaction of these compounds being closely connected with the structure of the latter. Hydrolysis of γ-silicon-containing vinyl ethers was run in 2% sulfuric acid [5]. The study showed that this reaction proceeds with formation of acetaldehyde and the γ-silicon-containing alcohol.

$$R_3SiCH_2CH_2CH_2OCH{=}CH_2 + H_2O \xrightarrow{H^+} CH_3CHO + R_3SiCH_2CH_2CH_2OH$$
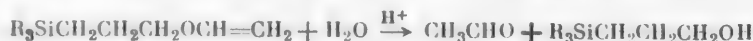
The mechanism of the hydrolysis of these ethers is evidently completely coincident with the mechanism of hydrolysis of vinyl alkyl ethers [6]. It was shown that the hydrolysis of γ-silicon-containing vinyl ethers proceeds to the extent of but 5-10% under the influence of 2% sulfuric acid under the usual conditions (duration of hydrolysis – 30 minutes), while the hydrolysis of the corresponding vinyl alkyl ethers proceeds quantitatively under the same conditions. An attempt to realize a complete hydrolysis of the former compounds under these conditions over the period of 24 hours failed to give the expected results. Hydrolysis proceeds to the extent of but 60-70% under such conditions. Heating to 100° for six hours is needed for the complete hydrolysis of these ethers.

The γ-silicon-containing vinyl ethers readily add various organic and organosilicon alcohols and silanols, forming organosilicon acetals [3-5].

$$R_3SiCH_2CH_2CH_2OCH{=}CH_2 + R'OH \rightarrow CH_3{-}CH{\begin{smallmatrix}OR' \\ OCH_2CH_2CH_2SiR_3\end{smallmatrix}}$$
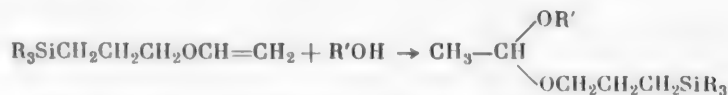
R = organic radical. R' = inorganic or organosilicon residue.

Catalysts – mineral acids and metal chlorides – aid the progress of this reaction. Hydrochloric acid acts most mildly. The reaction is exothermic, but has a smaller heat effect in comparison with the vinyl alkyl ethers. A series of perviously undescribed acetals, containing silicon atoms in both alcoholic radicals, was prepared in the course of this study.

$$R_3SiCH_2CH_2CH_2OCH{=}CH_2 + R'_3Si(CH_2)_nOH \xrightarrow{H^+} CH_3CH{\begin{smallmatrix}O(CH_2)_nSiR_3 \\ O(CH_2)_3SiR_3\end{smallmatrix}}$$

R & R'=CH₃ or C₂H₅, n=0, 1, 3.

Taking into account the Shostakovskii oxonium theory [1, 7, 8] and the generality of the conditions of formation of organic and organosilicon acetals, it is possible to consider that the addition reaction of hydroxyl containing compounds to the γ-silicon-containing vinyl ethers proceeds by the ionic mechanism [6] by the following scheme:

$$CH_2{=}CHO(CH_2)_3SiR_3 + HX \rightarrow CH_2{=}CHO(CH_2)_3SiR_3 \rightarrow$$
$$\underset{HX}{\vdots}$$

$$\rightarrow \left[\begin{array}{c} CH_2{=}CH \\ R_3Si(CH_2)_3 \end{array} {>}OH \right]^+ X^- \rightarrow CH_3{-}\overset{+}{C}HO(CH_2)_3SiR_3 + X^- \rightarrow$$

$$\rightarrow CH_3{-}\overset{+}{C}HO(CH_2)_3SiR_3 + R_3Si(CH_2)_nOH \rightarrow CH_3CH \underset{O(CH_2)_3SiR_3}{\overset{O(CH_2)_nSiR_3}{<}}$$
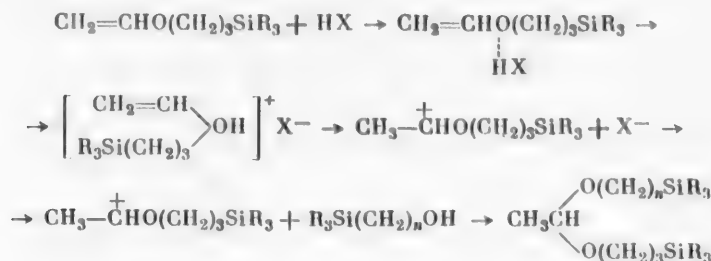
A study of the hydrolysis [5] of the resulting organosilicon acetals showed that it proceeds by the same scheme as does that of the organic acetals.

$$CH_3{-}CH \underset{O(CH_2)_3SiR_3}{\overset{O(CH_2)_nSiR_3}{<}} + H_2O \xrightarrow{H^+} CH_3{-}\overset{O}{\underset{H}{C{<}}} + R_3Si(CH_2)_3OH + R_3Si(CH_2)_nOH$$
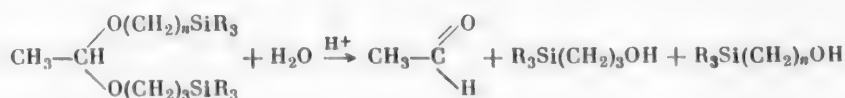
It was found thereupon that organosilicon acetals which contain siliconaatoms in both alcoholic radicals have a greater stability to hydrolysis than do the organosilicon acetals containing one silicon atom and even more than do the dialkyl acetals. The tendency of organosilicon acetals to hydrolysis is reduced with the symmetrization of these compounds. Therefore, introduction of silicon atoms into the alcoholic radicals of acetals raises their hydrolytic stability.

The addition reaction of monocarboxylic acids to γ-silicon-containing vinyl ethers was examined on the example of the reaction of the vinyl ether of γ-hydroxypropyltrimethylsilane with formic, acetic, propionic and isobutyric acids [5, 9]. The addition of saturated monocarboxylic acids to the vinyl ethers of γ-hydroxypropyltrimethylsilane led to the preparation of a series of representatives of a new class of organosilicon compounds — incomplete organosilicon acylals.

$$(CH_3)_3SiCH_2CH_2CH_2OCH{=}CH_2 + RCOOH \rightarrow CH_3{-}CH \underset{OCH_2CH_2CH_2Si(CH_3)_3}{\overset{OCOR}{<}}$$

$$R{=}H, \ CH_3, \ C_2H_5, \ C_3H_7{-} \ iso$$
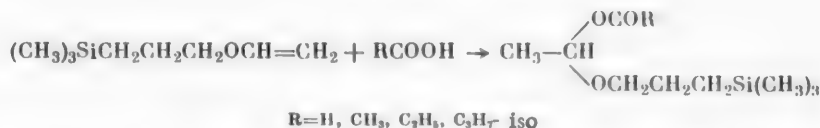
It was found thereupon that formic acid reacts very vigorously in the absence of a catalyst with the vinyl ether of γ-hydroxypropyltrimethyl silane. Addition of the other monocarboxylic acids is not observed without a catalyst under the usual conditions; a prolonged (30 hours) heating of the reaction mixture to 65-70° is necessary for their addition to the vinyl ether of γ-hydroxypropyltrimethylsilane. All the resulting organosilicon acylals, except for the acylal containing the residue of formic acid in its constitution, are characterized by the fact that they are more stable compounds than are their organic analogs.

The mechanism of formation of the incomplete organosilicon acylals from γ-silicon-containing vinyl ethers and monocarboxylic acids is also ionic and is evidently completely identical with the mechanism described by us for the organosilicon acetals.

$$CH_2{=}CHO(CH_2)_3SiR_3 + RCOOH \rightarrow CH_2{=}CHO(CH_2)_3SiR_3 \rightarrow$$
$$\underset{HOCOR}{\vdots}$$

$$\rightarrow \left[\begin{array}{c} CH_2{=}CH \\ R_3Si(CH_2)_3 \end{array} \!\!\!\!\! OH \right]^+ OCOR^- \rightarrow CH_3\overset{+}{C}HO(CH_2)_3SiR_3 + RCOO^- \rightarrow \begin{array}{c} \quad\quad OCOR \\ CH_3{-}CH \\ \quad\quad O(CH_2)_3SiR_3 \end{array}$$
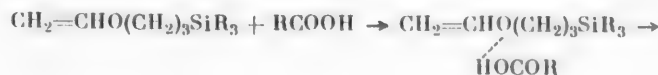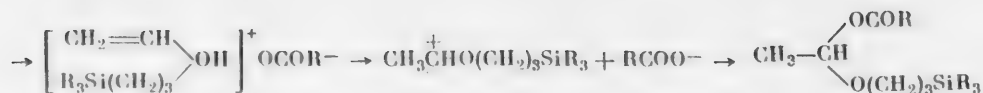
To prove the structure and to study the chemical properties of the resulting acylals we studied the reaction of hydrolysis of the latter [5]. It was established that the hydrolysis of incomplete organosilicon acylals is accompanied by the cleavage of the acylal into the γ-silicon-containing alcohol, acetyldehyde and organic acid.

$$\begin{array}{c} \quad\quad OCOR' \\ CH_3{-}CH \\ \quad\quad O(CH_2)_3SiR_3 \end{array} + H_2O \rightarrow R_3Si(CH_2)_3OH + CH_3{-}CHO + R'COOH$$
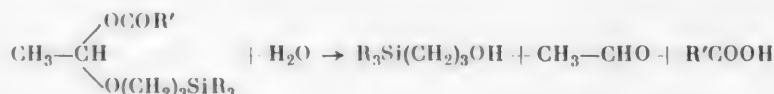
Organosilicon acylals turned out to be more stable to hydrolysis than their organic analogs. The stability of these compounds to hydrolysis increases with increased size of the acid radical of the acylal.

Halogenation of the γ-silicon-containing vinyl ethers was studied on the example of addition of chlorine to the vinyl ether of γ-hydroxypropylmethyldiethylsilane [10]. It was established during this study that the chlorination of γ-silicon-containing vinyl ethers leads to the formation of previously undescribed γ-silicon-containing α, β-dichloroethyl ethers according to the following scheme:

$$CH_2{=}CHO(CH_2)_3Si(C_2H_5)_2CH_3 + Cl_2 \rightarrow CH_2Cl{-}CHClO(CH_2)_3Si(C_2H_5)_2CH_3$$

The reaction is exothermic. The process of chlorination was run with cooling of the reaction mixture to $-5°$. Polymerization of the original vinyl ether and formation of products of deeper chlorination were not observed under such conditions. The resulting α, β-dichloro ether was a viscous colorless liquid which fumed slightly in air, decomposed in the presence of moisture and yellowed in light.

A study of the hydrolysis of α,β-dichloroethyl ether of γ-hydroxypropylmethyldiethylsilane showed that this substance is hydrolyzed very readily and quantitatively under the influence of water. The main hydrolysis products are chloroacetaldehyde, hydrochloric acid and γ-hydroxypropylmethyldiethylsilane.

$$CH_2Cl{-}CHClO(CH_2)_3Si(C_2H_5)_2CH_3 + H_2O \rightarrow$$
$$\rightarrow CH_2Cl{-}CHO + CH_3(C_2H_5)_2Si(CH_2)_3OH + HCl$$
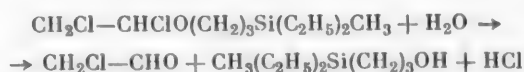
Chlorination of γ-silicon-containing vinyl ethers is a convenient and a very good method of synthesis of γ-silicon-containing α, β-dichloroethyl ethers.

Hydrohalogenation of γ-silicon-containing vinyl ethers was studied on the example of the addition reaction of hydrogen chloride and vinyl ether of γ-hydroxypropylmethyldiethylsilane [10]. A deep yellow, strongly fuming liquid with a penetrating choking odor was isolated as a result of the reaction. We failed to isolate the expected γ-silicon-containing α-chloroethyl ether owing to the instability of the latter.

For extension of the concepts about the properties of γ-silicon-containing vinyl ethers and for the proof of their structure we examined the reaction of hydrogenation of the latter [11]. The hydrogenation was run at atmospheric pressure over Raney nickel catalyst in ethyl alcohol medium; it proceeded smoothly with formation of γ-silicon-containing ethyl ethers, in yield of 97-98%, which were free of other impurities.

$$R_3SiCH_2CH_2CH_2OCH{=}CH_2 + H_2 \underset{Ni}{\rightrightarrows} R_3SiCH_2CH_2CH_2OC_2H_5$$
$$R{=}CH_3 \ \& \ C_2H_5.$$
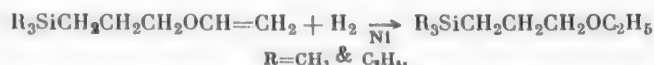
In this connection, the reaction of hydrogenation of γ-silicon-containing vinyl ethers may be made the foundation of a new method of preparation of γ-silicon-containing ethyl ethers.

The existence of the same regularities as in the organic series was discovered during the comparison of the physical properties of the γ-silicon-containing vinyl ethers and the corresponding ethyl ethers; specific gravities and indexes of refraction of the γ-silicon-containing ethyl ethers are lower than those of the corresponding vinyl ethers.

EXPERIMENTAL

The following silicon-containing vinyl ethers, prepared by us by the Favorskii-Shostakovskii method [3-5], were used:

vinyl ether of γ-hydroxypropyltrimethylsilane: b.p. 60-61° (18 mm), $n^{20}D$ 1.4625, d^{20}_4 0.8171; vinyl ether of γ-hydroxypropylmethyldiethylsilane: b.p. 82-83° (8 mm), $n^{20}D$ 1.4415, d^{20}_4 0.8326; vinyl ether of γ-hydroxypropyltriethylsilane: b.p. 69-70° (3 mm), $n^{20}D$ 1.4453, d^{20}_4 0.8409.

TABLE 1

Hydrolysis of Organosilicon Vinyl Ethers (Time of hydrolysis 30 minutes; temperature 20°)

Formula of ether	P	a	b	$a-b$	F	Ether found (in %)
$(CH_3)_3SiCH_2CH_2CH_2OCH{=}CH_2$	0.24015	31.05	29.60	1.45	0.978	4.68
	0.23115	31.05	29.30	1.75	0.978	5.86
$CH_3(C_2H_5)_2SiCH_2CH_2CH_2OCH{=}CH_2$	0.19685	31.05	29.50	1.55	0.978	7.18
	0.17020	31.05	30.00	1.05	0.378	5.62
$(C_2H_5)_3SiCH_2CH_2CH_2OCH{=}CH_2$	0.21020	31.05	29.75	1.30	0.978	6.06
	0.19365	31.05	29.50	1.55	0.978	7.85

TABLE 2

Hydrolysis of γ-Silicon-Containing Vinyl Ethers on Boiling (Time of hydrolysis 6 hours)

Formula of ether	P	a	b	$a-b$	F	Ether, found (in %)
$(CH_3)_3Si(CH_2)_3OCH{=}CH_2$	0.2606	30.475	23.075	7.400	0.9997	97.4
	0.2181	30.475	23.80	6.675	0.9997	96.9
$CH_3(C_2H_5)_2Si(CH_2)_3OCH{=}CH_2$	0.1392	24.15	30.67	3.48	1.013	96.21
	0.1212	32.40	29.30	3.10	1.005	95.80
	0.1465	32.40	28.65	3.75	1.005	95.85
$(C_2H_5)_3Si(CH_2)_3OCH{=}CH_2$	0.1307	32.05	29.03	3.02	0.9997	92.58
	0.1365	32.05	28.80	3.25	0.9997	95.40

Hydrolysis of γ-silicon-containing vinyl ethers was run under the influence of 2% sulfuric acid. Acetaldehyde in the hydrolyzate was determined by the bisulfite method [12]. Hydrolysis at room temperature was run by the following technique. A sample of the organosilicon vinyl ether being studied was sealed in a thin-walled ampul and placed into a flask with a ground-in stopper, the flask containing 25 ml of 2% sulfuric acid and 20 ml of 0.1N sodium bisulfite solution. The ampul was broken, the flask was shaken energetically for 15 minutes and, after a 15-minute standing, the flask contents were titrated with 0.1N iodine solution. The calculation was done with the formula:

$$\% \text{ ether } = \frac{M \cdot (a-b) \cdot F \cdot 100}{2 \cdot 10 \cdot 1000 \cdot P} = \frac{M \cdot (a-b) \cdot F}{200 \cdot P},$$

where: a — iodine number of 25 ml 0.1N bisulfite expressed in ml of 0.1N iodide solution; b — number of milliliters of 0.1N iodine solution used for back-titration; F — factor of the iodine solution; P — sample weight; M — molecular weight of the ether.

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TABLE 3

No.of compound	Formula of compound (see below)	Name of compound	B. p. (pressure in mm)
1	$(CH_3)_3SiCH_2CH_2CH_2OH$	γ-Hydroxypropyltrimethylsilane	80° (24)
2	$CH_3(C_2H_5)_2SiCH_2CH_2CH_2OH$	γ-Hydroxypropylmethyldiethylsilane	98 (10) 102—103 (12)
3	$(C_2H_5)_3SiCH_2CH_2CH_2OH$	γ-Hydroxypropyltriethylsilane	80—81 (3)
4	$(CH_3)_3SiCH_2CH_2CH_2OCH=CH_2$	Vinyl ether of γ-hydroxypropyltrimethylsilane	61 (18)
5	$CH_3(C_2H_5)_2SiCH_2CH_2CH_2OCH=CH_2$	Vinyl ether of γ-hydroxypropylmethyldiethylsilane	82—83 (8)
6	$(C_2H_5)_3SiCH_2CH_2CH_2OCH=CH_2$	Vinyl ether of γ-hydroxypropyltriethylsilane	69—70 (3)
7	$(CH_3)_3SiCH_2CH_2CH_2OC_2H_5$	Ethyl ether of γ-hydroxypropyltrimethylsilane	153 (749)
8	$CH_3(C_2H_5)_2SiCH_2CH_2CH_2OC_2H_5$	Ethyl ether of γ-hydroxypropylmethyldiethylsilane	62 (3)
9	$CH_3(C_2H_5)_2SiCH_2CH_2CH_2OCHClCH_2Cl$	α,β-Dichloroethyl ether of γ-hydroxypropylmethyldiethylsilane	113—114 (2.5)
10	$CH_3-CH\begin{matrix}OC(CH_3)_2C\equiv CH\\OCH_2CH_2CH_2Si(CH_3)_3\end{matrix}$	3,3-Dimethyl-1-propynyl 1-trimethylsilylpropyl acetal	105—107 (7.5)
11	$CH_3-CH\begin{matrix}OSi(C_2H_5)_3\\OCH_2CH_2CH_2Si(CH_3)_3\end{matrix}$	Triethylsilyl trimethylsilylpropyl acetal	132 (9)
12	$CH_3-CH\begin{matrix}OCH_2Si(CH_3)_3\\OCH_2CH_2CH_2Si(CH_3)_3\end{matrix}$	Trimethylsilylmethyl trimethylsilylpropyl acetal	107—108 (6)
13	$CH_3-CH[OCH_2CH_2CH_2Si(CH_3)_3]_2$	Bis-(trimethylsilylpropyl) acetal	126—127 (6)
14	$CH_3-CH\begin{matrix}OCH_2CH_2CH_2Si(CH_3)_3\\OCH_2CH_2CH_2Si(C_2H_5)_2CH_3\end{matrix}$	Trimethylsilylpropyl methyldiethylsilylpropyl acetal	140—141 (3) 131—132 (2)
15	$CH_3-CH[OCH_2CH_2CH_2Si(C_2H_5)_2CH_3]_2$	Bis-(methyldiethylsilylpropyl) acetal	156—157 (2)
16	$CH_3CH\begin{matrix}OCOH\\OCH_2CH_2CH_2Si(CH_3)_3\end{matrix}$	Trimethylsilylpropoxyethylidene formate	80—81 (8)
17	$CH_3-CH\begin{matrix}OCOCH_3\\OCH_2CH_2CH_2Si(CH_3)_3\end{matrix}$	Trimethylsilylpropoxyethylidene acetate	92—93 (8)
18	$CH_3-CH\begin{matrix}OCOCH_2CH_3\\OCH_2CH_2CH_2Si(CH_3)_3\end{matrix}$	Trimethylsilylpropoxyethylidene propionate	99—100 (7)
19	$CH_3-CH\begin{matrix}OCOC_3H_7\text{-iso}\\OCH_2CH_2CH_2Si(CH_3)_3\end{matrix}$	Trimethylsilylpropoxyethylidene isobutyrate	110—111 (3)

n_D^{20}	d_4^{20}	MR$_D$ found	MR$_D$ calc.	Empirical formula	% C found	% C calc.	% H found	% H calc.	% Si found	% Si calc.	Yield (in %)
1.4296	0.8405	--	-	$C_6H_{10}OSi$	...	--	- -	...	--	--	77
1.4452	0.8489	50.28	50.35	$C_8H_{20}OSi$	60.24, 60.18	59.94	12.52, 12.74	12.57	18.29, 18.49	17.50	68
1.4536	0.8565	55.09	54.98	$C_9H_{22}OSi$	62.04, 61.99	61.99	12.82, 12.74	12.72	—	—	58.9
1.4265	0.8171	49.69	50.10	$C_8H_{18}OSi$	60.58, 60.41	60.69	11.59, 11.48	11.46	17.34	17.72	63.2
1.4415	0.8326	59.80	59.36	$C_{10}H_{22}OSi$	64.05, 64.20	64.45	12.11, 11.94	11.90	15.80, 15.98	16.06	64.5
1.4453	0.8409	63.61	63.99	$C_{11}H_{24}OSi$	65.51, 65.43	65.92	12.21, 12.19	12.17	14.31, 14.22	14.02	59.6
1.4144	0.7932	50.55	50.57	$C_8H_{20}OSi$	—	...	—	..	—	—	98.7
1.429~	0.8168	59.56	59.83	$C_{10}H_{24}OSi$	63.20, 63.07	63.75	12.64, 12.68	12.84	15.61, 15.55	14.91	96.8
1.4725	1.0418	69.22	69.51	$C_{10}H_{22}OSiCl_2$	44.86, 45.01	46.62	8.21, 8.27	8.62	11.28, 11.53	10.92	79.8
1.4319	0.8480	74.44	73.88	$C_{13}H_{26}O_2Si$	64.32, 64.55	64.41	10.90, 10.84	10.81	10.53, 10.72	11.57	56.0
1.4362	0.8653	87.83	87.74	$C_{14}H_{34}O_2Si_2$	58.58, 58.43	57.87	11.82, 11.89	11.80	19.06, 19.06	19.31	60.0
1.4271	0.8408	80.17	80.49	$C_{12}H_{30}O_2Si_3$	55.65, 55.71	54.90	11.52, 11.52	11.52	21.05, 20.75	21.38	58.4
1.4350	0.8549	88.67	89.75	$C_{14}H_{34}O_2Si_2$	57.67, 57.61	57.87	11.65, 11.66	11.80	19.03, 18.98	19.31	63.3
1.4425	0.8589	98.26	99.01	$C_{16}H_{38}O_2Si_2$	59.87, 59.93	60.30	12.04, 11.93	12.02	17.00, 17.37	17.63	61.5
1.4492	0.8666	107.42	108.27	$C_{18}H_{42}O_2Si_2$	61.96, 61.91	62.31	12.19	12.20	16.25, 16.46	16.19	62.2
1.4252	0.8903	58.58	56.97	$C_9H_{20}O_3Si$	—	—	—	..	14.10, 13.74	13.56	52.6
1.4218	0.9027	61.44	61.60	$C_{10}H_{22}O_3Si$	55.36, 55.27	54.97	10.35, 10.34	10.11	12.61, 12.84	12.85	59.2
1.4242	0.8975	66.23	66.07	$C_{11}H_{24}O_3Si$	56.66, 56.75	56.85	10.40, 10.38	10.41	12.01, 12.26	12.08	73.2
1.4639	0.9675	70.56	70.86	$C_{12}H_{26}O_3Si$	58.36, 58.22	58.48	10.56, 10.44	10.64	11.48, 11.50	11.40	64.0

The results of the hydrolysis of γ-silicon-containing vinyl ethers under these conditions are given in Table 1.

The hydrolysis of the organosilicon vinyl ethers with heating was run in the following manner. 20 ml 2% sulfuric acid and a sample of the ether were placed in a thin-walled ampul, into an ampul with 150 ml volume. The large ampul was sealed, the small ampul was broken by strong shaking and the ampul was heated in a boiling water bath for six hours. The ampul contents were quantitatively transferred, after being cooled, into a volumetric flask with 200 ml capacity, and the solution volume was made up to the mark by addition of distilled water. The determination of acetaldehyde content was run after good mixing. For this, 15 ml of 0.1N sodium bisulfite solution was added to 50 ml of the prepared solution, the mixture was thoroughly mixed and, after a 15-minute standing period, the excess bisulfite was titrated with 0.1N iodine solution. The results of the hydrolysis of organosilicon vinyl ethers under such conditions are given in Table 2.

Synthesis of triethylsilyl trimethylsilylpropyl acetal. 10 g (0.064 mole) of vinyl ether of γ-hydroxy-propyltrimethylsilane and 8.4 g (0.064 mole) of triethylsilanol were placed in a three-necked round-bottomed flask of 25 ml capacity. 0.02 ml of 30% hydrochloric acid was added with energetic stirring, whereupon a temperature rise to 49° was observed. The reaction mixture was heated at 55° for 30 min,was left overnight and on the following day was neutralized with potassium carbonate and subjected to a distillation. 12 g (66%) of the acetal was isolated.

B.p. 132° (9 mm), $n^{20}D$ 1.4362, d^{20}_4 0.8653, MR_D 87.82; Calculated 87.74.
Found %: C 58.58, 58.43; H 11.82, 11.89; Si 19.06, 19.06, M 270.8, 267.1. $C_{14}H_{34}O_2Si_2$. Calculated % C 57.87; H 11.80; Si 19.34. M 290.

A series of organosilicon acetals, whose physicochemical constants are given in Table 3, was prepared by the above-described technique.

SUMMARY

1. Vinylation reaction of γ-silicon-containing alcohols by the method of Favorskii-Shostakovskii was studied. It was shown that the usual method of vinylation under the influence of potassium hydroxide is unsatisfactory. The use of alcoholates of these alcohols for the catalysts aids the vinylation reaction. The optimum conditions were found on this basis and a method of synthesis of γ-silicon-containing vinyl ethers was developed.

2. Addition of alcohols, silanols and organic acids to γ-silicon-containing vinyl ethers under the influence of acidic catalysts proceeds by an ionic mechanism in accord with the Markovnikov rule. Their reaction with organosilicon alcohols and silanols yielded the previously undescribed acetals containing silicon atoms in both alcoholic radicals. The reaction of these ethers with organic acids may be used as the basis for the preparation of a new class of organosilicon compounds — incomplete organosilicon acylals.

3. Hydrogenation, chlorination and hydrochlorination of γ-silicon-containing vinyl ethers were studied.

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THE STRUCTURE OF BUTADIENE POLYMER FORMED IN THE PRESENCE OF AN ALFIN CATALYST

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The process of polymerization of diene hydrocarbons with a conjugated double bond system proceeds under the influence of alkali metals or of their organic compounds in such a manner that the addition of the monomer takes place at the end of the polymer chain at the C-metal bond. Hence, the structure of the polymer chain is determined by the nature of the metal [1]. In the polymerization of 1,3-butadiene in the presence of metallic sodium or organosodium compounds the amount of the 1,2-links in the polymer chain reaches 70%; in the presence of potassium it reaches 35%; and in the presence of lithium – 25% [2, 5]. Morton showed that the polymerization of 1,3-butadiene in the presence of an alfin catalyst [3], which is a complex of an organometallic compound with some other component (for example, a combination of allylsodium, sodium isopropoxide and sodium chloride), occurs predominantly in 1,4-position and the resulting polymers have a regular structure in the opinion of the author [4].

The present study had for its goal a study of the chemical structure of 1,3-butadiene polymer prepared in the presence of an alfin catalyst. A soluble part was separated from the insoluble part of the polymer and for each of these we ran an ozonization, an oxidative decomposition of the ozonide by acetyl hydroperoxide and a separation of the resulting acids by means of partition chromatography. The chromatogram of the ozonolysis products of the insoluble part of the polymer, obtained in the presence of an alfin catalyst (Fig. 2, solid line), differed but little from the chromatogram of the ozonolysis products of the soluble part of this polymer (Fig. 1). The carbon skeleton of the polymer is somewhat more fully accounted for in the latter case, but the relative amounts of each acid in the acid mixture of the ozonolysis products remain the same. In the table, we give the data on the accounting for the carbon skeleton in various regions of the polymer macromolecule prepared in the presence of an alfin catalyst. The chemical structure of this polymer differs from the chemical structure of the sodium-butadiene rubbers. A greater percentage of the carbon skeleton of the polymer prepared in the presence of the alfin catalyst is accounted for by 1,4-links; the percentage of the 1,2-links is greatly reduced.

Five peaks are located on the chromatograms of the ozonolysis products of the soluble and the insoluble parts of the polymer being studied (Figs. 1 and 2), of which four represent known acids. The chromatograms terminate in the peak which corresponds to 1,2,3-propanetricarboxylic acid. Succinic and 1,2,4-butanetricarboxylic acids are normal ozonolysis products of the 1,4-1,4 and 1,4-1,2-1,4 regions of the polymer chain [5]. 1,2,3-Propanetricarboxylic acid could have formed from the 1,4-1,4-regions of the polymer chain which are branched at the α-methylene group. On the other hand, this acid could have originated from the 1,4-1,2-1,4-regions of the polymer chain as an anomalous ozonolysis product as the result of chain shortening of the 1,4-1,2-1,4-regions through the attack by ozone on the α-methylene group [6]. It was shown that an anomalous product – 1,2,3-propanetricarboxylic acid – is found in the amount of 3%, based on the carbon skeleton of 1-vinyl-3-cyclohexene [7], in the ozonolysis products of 1-vinyl-3-cyclohexene, which is the model for the 1,4-1,2-1,4-region of the polymer chain. Acetic acid cannot be included into the consideration since the oxidative decomposition of the ozonides was run in acetic acid medium and for this reason acetic acid could have partially remained among the ozonolysis products. The chromatograms of the ozonolysis products of the

Acid	Acid in ozonolysis products (in g)		Percentage of carbon of the rubber accounted for by the given acid		Region of the polymer chain	Percentage of carbon in the region	
	soluble part	insoluble part	soluble part	in insoluble part		soluble part	insoluble part
Succinic	2.10	1.86	41.2	35.8	1,4-1,4	41.2	35.8
1,2,4-Butanetricarboxylic	0.54	0.47	11.4	9.8	1,4-1,2-1,4	13.0	11.2
1,2,3-Propanetricarboxylic	0.41	0.35	8.2	6.8	1,4-1,2-1,4	1.0	•
					1,4-1,4 branched at the α-methylene group	7.2	•

•The percentage of carbon in the 1,4-1,2-1,4 and 1,4-1,4 regions, branched at the α-methylene group, was not calculated for the insoluble part of the polymer owing to the fact that the content of 1,2-links for this part of the polymer was not determined.
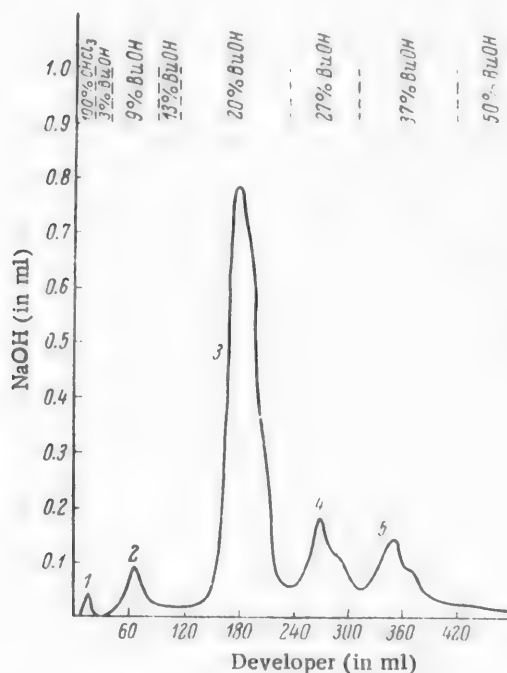
Fig. 1. Chromatogram of ozonolysis products of the soluble part of the polymer prepared in the presence of an alfin catalyst: 1) not identified, 2) acetic acid, 3) succinic acid, 4) 1,2,4-butanetricarboxylic acid, 5) 1,2,3-propanetricarboxylic acid.

polymer prepared in the presence of an alfin catalyst are relatively simple in comparison with the chromatograms of the ozonolysis products of sodium-butadiene rubbers [5]. It follows from the examination of these chromatograms (Figs. 1 and 2) that the macromolecules of the polymer contain only the 1,4-1,4; 1,4-1,2-1,4; and 1,4-1,4 regions branched at the α-methylene group. 1,x,y,6-Hexanetetracarboxylic acid, which could have indicated the presence of 1,4-(1,2)$_2$-1,4 regions in the polymer, and more complex acids, were absent from this polymer's ozonolysis products. Consequently, the losses of the carbon skeleton during the ozonolysis of the polymer obtained in the presence of the alfin catalyst may be explained by an abnormal ozonolysis of the 1,4-1,4; 1,4-1,2-1,4; and 1,4-1,4 regions branched at the α-methylene group.

EXPERIMENTAL

The polymer being studied was prepared in petroleum ether with the molar ratio of monomer: initiator of 180:1. The polymerization was run at 20°. The main catalyst components were allylsodium, sodium chloride and sodium isopropoxide. The glazing temperature of the polymer was −72°.• The soluble part of the polymer was separated from the insoluble part by extraction with benzene. The soluble part was precipitated from the benzene solution with ethyl alcohol. Both forms of the thus purified polymer were dried at 30-34° (3 mm) to a constant weight. The purification of the polymer was done in the atmosphere of oxygen-free nitrogen. For the soluble part of the polymer we found: C 88.40%; H 10.90% and

•The polymer was prepared at the S.V. Lebedev All-Union Research Institute for Synthetic Rubber.

determined the percentage of the 1,2-links by the amount of formaldehyde and formic acid in the decomposition products of the polymer ozonide with water [2]. 16.2% of the carbon skeleton of the polymer was located in the 1,2-links.

The oxidative decomposition of the polymer ozonide with acetyl hydroperoxide was run under the same conditions for the soluble and the insoluble parts of the polymer. Ethyl acetate was used as the solvent during the ozonization. The ozonization was run at −25°. The solvent was distilled from the ozonide at 23° (10 mm). The ozonide was decomposed with acetyl hydroperoxide in glacial acetic acid. The excess of the hydroperoxide was destroyed with platinum black until the hydroperoxide test with potassium iodide became negative. No aldehydes were detected in the solution of the ozonolysis products in acetic acid. The acetic acid was distilled at 35° (3 mm).

2.40 g of the insoluble part of the polymer and 2.35 g of the soluble part were ozonized. 3.70 g of acidic products of ozonolysis of the insoluble part was obtained (% C 39.43, % H 5.26) and 3.93 g of the ozonolysis products of the soluble part (% C 41.67, % H 4.72). The acids were separated by the technique of partition chromatography [5-8]. The results of the chromatography are shown graphically. The elution peaks on the chromatograms characterize the acids which make up the mixture. The chromatograms which were obtained in the separation of the acidic products of ozonolysis were compared with the chromatogram of a mixture of the expected acids prepared under the same conditions (Fig. 2, dotted line).

74.5% of the carbon skeleton was accounted for in the products of oxidative decomposition of the soluble part of the polymer under study with acetyl hydroperoxide. The disagreement of the amount of the carbon skeleton accounted for by the elemental analysis of the ozonolysis products and the amount of the carbon skeleton contained in the regions of the polymer chain known to us (62.4%, see table) is most readily

Fig. 2. Chromatogram of the ozonolysis products of the insoluble part of the polymer prepared in the presence of the alfin catalyst: 1) not identified, 2) acetic acid, 3) succinic acid, 4) 1,2,4-butanetricarboxylic acid, 5) 1,2,3-propanetricarboxylic acid. The dotted line shows the chromatogram of the mixture of the following acids: 2) acetic, 3) succinic, 4) 1,2,4-butanetricarboxylic, 5) 1,2,3-propanetricarboxylic.

explained by the presence of neutral substances among the ozonolysis products, these being the abnormal ozonolysis products which could not be accounted for during the chromatography.

Since in this polymer all the 1,2-links enter the 1,4-1,2-1,4 region of the polymer chain, it is possible to calculate what part of the polymer hydrocarbon is contained in the 1,4-1,2-1,4 regions, from the amount of the carbon skeleton contained in the 1,2-links. 16.2% of the carbon skeleton was experimentally located in the 1,2-links, by the amount of formic acid and formaldehyde in the ozonolysis products of the soluble part of the polymer. Therefore, 32.4% of the carbon skeleton or 0.67 g of carbon (for 2.08 g of carbon, corresponding to 2.35 g of the polymer) is contained in the 1,4-1,2-1,4-region. About 3% [7], or 0.02 g of carbon, of the 1,4-1,2-1,4-region (from 0.67 g of carbon) is subjected to the abnormal ozonolysis with formation of 1,2,3-propanetricarboxylic acid. 0.41 g of the latter was experimentally found among the ozonolysis products (see table), i.e., 0.17 g of carbon. This amounts to 8.2% of 2.08 g of carbon in the polymer. Thus, from 8.2% of carbon accounted for by the 1,2,3-propanetricarboxylic acid, the share of the 1,4-1,2-1,4-regions which suffered the abnormal ozonolysis is 1% of carbon (0.02 g of carbon for 2.08 g of carbon in the polymer), while 7.2% of carbon falls to the share of the 1,3-1,4-region branched at the α-methylene group.

SUMMARY

1. The butadiene polymer prepared in the presence of an alfin catalyst contains 16.2% of 1,2-links, while the butadiene rubber prepared in the presence of metallic sodium contains up to 70% of 1,2-links.

2. The polymer which was examined has a simpler structure of the polymer chain than does the rubber prepared in the presence of metallic sodium. It contains only the 1,4-1,4; 1,4-1,2-1, 1,4 and 1,4-1,4-regions branched at the α-methylene group. The amount of the carbon skeleton contained in the 1,4-1,4-regions branched at the α-methylene groups is 7.2%.

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A STUDY IN THE FIELD OF CYCLIC ACETALS OF HYDROXY CARBONYL COMPOUNDS.

IX. ETHYL-LACTOLIDES AND DIETHYL KETALS OF ETHYLBENZOYLCARBINOL AND PROPYLBENZOYLCARBINOL

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Over the eight years since the publication of the first paper dealing with the chemistry of new derivatives of α-oxo alcohols – their methyl-lactolides [1] – a considerable amount of experimental material has been accumulated in this field. It has been shown [2, 3] that methyl-lactolides (I) react readily with various reagents yielding various derivatives of α-oxo alcohols; here, the oxide ring is broken in the predominant majority of cases at the carbon atom at which the methoxy group is attached.
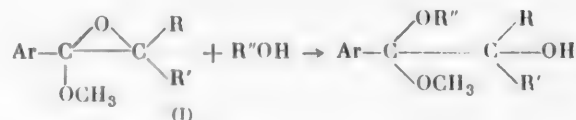
The degree of stability of the primary reaction product and its ability to undergo further transformations under the conditions of the process (or during the isolation of the pure substance) determine the composition and the structure of the substances formed as the final result [1-3]. Methyl-lactolides of α-oxo alcohols are formed by the action of sodium methoxide suspension on α-bromo ketones in absolute ether. If the reaction is run in methyl alcohol, usually the dimethyl ketals of α-oxo alcohols are formed and only with the relatively unreactive methyl-lactolides is it possible to isolate the latter. The stability of the methyl-lactolides of tertiary α-oxo alcohols is considerably greater than the stability of the same derivatives of secondary α-oxo alcohols.

The ethyl-lactolides of α-oxo alcohols are almost completely unstudied. Their sole representative – methyl-lactolide of dimethylbenzoylcarbinol (Ar = C_6H_5; R and R' = CH_3) has been described briefly [4]; despite its haveing been prepared in a considerable quantity, there is only the indication that it is transformed into the corresponding esters of dimethylbenzoylcarbinol by its reaction with benzoic and p-nitrobenzoic acids. The still earlier data on the preparation of ethyl-lactolides [5] turned out to have been erroneous and were later retracted [4]. It is possible to expect theoretically that ethyl-lactolides should be more reactive than the methyl-lactolides in such reaction in which the rate is determined by the rate of opening of the oxide ring under the influence of catalysts of the acid type, since the +C effect of the ethoxy group is somewhat greater than the +C effect of the methoxy group.

Two new representatives of ethyl-lactolides of secondary alkaromatic α-oxo alcohols – ethylbenzoylcarbinol and propylbenzoylcarbinol – were prepared in this work, starting with α-bromopropyl phenyl ketone and α-bromobutyl phenyl ketone. Very considerable tar formation was observed when this reaction was run in the usual way – by the action of a suspension of sodium ethoxide in absolute ether.

$$C_6H_5-\underset{\underset{O}{\|}}{C}-CHBr-R \xrightarrow{C_2H_5ONa} C_6H_5-\underset{\underset{OC_2H_5}{|}}{C}\overset{O}{\diagup\diagdown}CH-R \quad (II)$$

where R = C_2H_5 or C_3H_7.
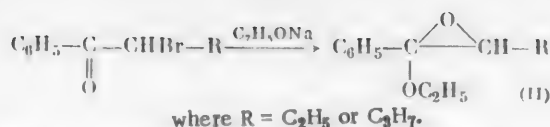
Both ethyl-lactolides (II) are readily mobile liquids in the freshly-distilled state, and have a pleasant fruity odor. The yield is but 10-15%. (Methyl-lactolides of the same oxo alcohols are prepared in 40-60% yields). The stability of the ethyl-lactolides is quite low, their odor changes rapidly to a penetrating, unpleasant one, the index of refraction rises and the percent content of the ethoxy group drops. An instant hydrolysis of the ethyl-lactolide of ethylbenzoylcarbinol, with formation of ethylbenzoylcarbinol, occurs in its reaction with water in an alkaline medium.

Almost no tar formation occurs in the reaction of sodium ethoxide and the same bromo ketones in anhydrous alcohol solution; however, it was possible to isolate the corresponding ethyl-lactolide (II, R = C_3H_7) only by starting with α-bromobutyl phenyl ketone, running the reaction in the cold and working up the reaction mixture very rapidly. Either diethyl ketals of the corresponding α-oxo alcohols (III), or the transformation products of the latter, whose nature is determined by the size of the hydrocarbon group R, and by the conditions of running the reaction and of isolating of the products, are formed if the reaction mixture is allowed to stand. Thus, in the reaction of α-bromopropyl phenyl ketone with sodium ethoxide in an alcoholic solution with heating there is formed not the diethyl ketal but the cyclo-diethyl-lactolide of ethylbenzoylcarbinol (IV, R=C_2H_5):

$$C_6H_5-\underset{\underset{OC_2H_5}{|}}{\overset{\overset{OC_2H_5}{|}}{C}}-CHOH-R$$

(III)

(IV)
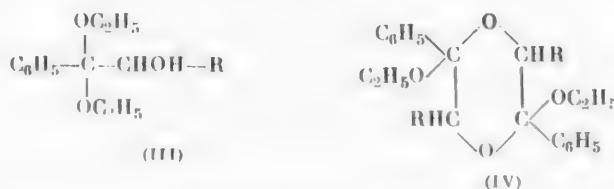
The same cyclodiethyl-dilactolide was obtained for identification by the action of a 2% solution of hydrogen chloride in anhydrous alcohol on ethylbenzoylcarbinol, by analogy with the well-known method of preparation of methylglucosides developed by E. Fischer and that of preparation of cyclodimethyldilactolides of α-oxo alcohols of the alkaromatic series [6].

Diethyl ketals (III, R = C_2H_5 or n-C_3H_7) are obtained only if the reaction is run in the cold; only the diethyl ketal of ethylbenzoylcarbinol could be isolated in an analytically pure state after distillation in high vacuum (0.3 mm). The latter proved to be very poorly stable in storage without a solvent and after but two hours after its isolation, the formation of a crystalline substance became noticeable and after several hours the entire substance solidified to an almost complete mass of crystals which turned out to be the cyclo-diethyl-dilactolide of ethylbenzoylcarbinol (IV, R = C_2H_5). Such transformations have been often observed among the dimethyl ketals of α-oxo alcohols but usually only during prolonged storage [7, 8]. It was noted that their tendency of change into the dioxane derivatives declines with increased chain length of the hydrocarbon groups [8]. Similarly in our case the ketal of the next homolog of the α-oxo alcohol – diethyl ketal of propylbenzoylcarbinol (III, R = C_3H_7) slowly changed into the corresponding cyclo-diethyldilactolide. Both diethyl ketals are poorly stable at elevated temperature; during attempts to distill them under 3-7 mm vacuum we invariably obtained mixtures of substances which differed more and more in composition from the ketal upon repeated distillations. The decomposition of the diethyl ketals at elevated temperature proceeded mainly in the direction of formation of ethoxy ketones – ethyl ethers of the isomeric α-oxo alcohols, while α-oxo alcohols were obtained in insignificant amounts.

$$(III) \rightarrow C_6H_5-\underset{\underset{OC_2H_5}{|}}{CH}-CO-R + C_6H_5-CO-CHOH-R$$
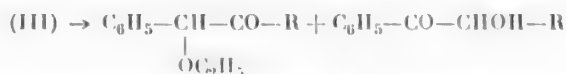
Diethyl ketal of propylbenzoylcarbinol was subjected to a complete decomposition by a prolonged heating under vacuum at 120-130° in order to isolate one of the ethoxy ketones (R = C_3H_7) in the pure state. The

ethereal solution of the decomposition products was repeatedly shaken with water to a negative reaction with
Fehling solution in order to remove the accompanying α-oxo alcohol. The ethoxy ketone was characterized
as its 2,4-dinitrophenylhydrazone while the presence in the ketone of a carbonyl group that is not conjugated
with the benzene ring was shown spectroscopically (the infrared spectrum showed the characteristic band at
1723 cm^{-1}). Similarly, the infrared spectrum of α-ethoxybenzyl ethyl ketone contained the band at 1725 cm^{-1}.
Similar transformations were also observed for the dimethyl ketals, but only during their distillation in the
presence of acetic anhydride or potassium bisulfate [9].

In the present work we made an attempt to prepare the ethoxy ketone (IV, R = C_3H_7) by isomerization
of ethyl-lactolide (II, R = n-C_3H_7) by an analogy with the isomerizations of methyl-lactolides which had been
well studied in a series of papers [10]. However, during the heating of the ethyl-lactolide with zinc chloride
a dimerization took place, rather than an isomerization, and this yielded the cyclo-diethyl-dilactolide of pro-
pylbenzoylcarbinol (IV, R = C_3H_7).

Thus, ethyl-lactolides and diethyl ketals of alkaromatic α-oxo alcohols are considerably less stable than
are the corresponding methyl derivatives.

EXPERIMENTAL

1. Action of sodium ethoxide on α-bromopropyl phenyl ketone in alcoholic solution. 16 g of α-bromo-
propyl phenyl ketone was added gradually and with constant stirring to a solution of sodium ethoxide (1.6 g of
sodium, 40 ml of anhydrous alcohol). A precipitate of sodium bromide began to separate immediately while
the solution acquired a light cherry color; the color faded over 1.5-2 hours and the solution became yellow.
The subsequent treatment of the reaction mixture was run under different conditions.

a) The reaction mixture was heated to 30-50° for eight hours, after which it was set aside for three days
longer. A loose crystalline precipitate began to separate from the solution on the second day, this differing
greatly in its density from the sodium bromide precipitate which remained on the bottom of the flask. The
crystals were separated and washed with alcohol, then with water (to remove the sodium bromide). The same
crystalline substance, which turned out to be the cyclo-diethyl-dilactolide of ethylbenzoylcarbinol was obtained
from the alcoholic mother liquor after the main bulk of the solvent had been distilled; this was sparingly solu-
ble in methyl and ethyl alcohols, somewhat better in ether and in benzene from which it could be recrystallized;
m.p. 190-191°.

Found %: C 74.63, 74.77; H 8.33, 8.45; OC_2H_5 23.02, 23.32. $C_{24}H_{32}O_4$. Calculated %: C 75.0;
H 8.33; OC_2H_5 23.43.

2.1 g of a light yellow liquid with b.p. 109-111° at 6 mm, which turned out to be a mixture of ethylben-
zoylcarbinol and its diethyl ketal, was isolated from the mother liquor after separation of the crystals. On heat-
ing of this mixture with an excess of alcoholic solution of 2,4-dinitrophenylhydrazine (with addition of sulfuric
acid) we obtained the osazone of ethylbenzoylcarbinol in the form of a fine red powder with m.p. 234-236°.

Found %: N 20.99, 21.22. $C_{22}H_{18}O_8N_8$. Calculated %: N 21.45.

b) In order to isolate the primary reaction product − diethyl ketal of ethylbenzoylcarbinol − in the pure
state, the reaction was run without heating, when the negative test for halogen in the organic matter was obtain-
ed only after seven days. Sodium bromide was filtered off and the alcohol was distilled off under vacuum. The
residue was vacuum distilled. Six g of the substance with b.p. 75° at 0.3 mm was isolated from 16 g of the
initial bromo ketone.

d^{20}_4 1.006, n^{20}D 1.4905, MR_D 68.4; Calculated, 68.06.
Found %: C 70.31, 70.49; H 9.32, 9.34; OH 6.95, 7.25. $C_{14}H_{22}O_3$. Calculated %: C 70.59; H 9.24;
OH 7.1

After approximately two hours we observed the formation of crystals and soon the whole froze to a solid
mass of crystals which were identical with the crystals isolated in experiment a.

Diethyl ketal of ethylbenzoylcarbinol decomposed during the running of the process under the same con-
ditions but with the distillation of the reaction product being performed under poorer vacuum (4-7 mm). Ethyl
ether of the isomeric oxo alcohol − phenylpropionylcarbinol (ethyl α-ethoxybenzyl ketone) − was isolated in

an almost pure state by repeated distillations; b.p. 114° at 5 mm, $n^{20}D$ 1.5055.

Found %; C 74.38; H 8.05. $C_{12}H_{16}O_2$ Calculated %: C 75.00; H 8.33.

The 2,4-dinitrophenylhydrazone of the ethoxy ketone formed golden yellow needle-shaped crystals (from alcohol) with m.p. 127-128°.

Found %: N 15.35, 15.22; OC_2H_5 12.08, 12.38. $C_{18}H_{20}O_5N_4$. Calculated %: N 15.05; OC_2H_5 12.09.

2. Action of sodium ethoxide on α-bromopropyl phenyl ketone in the medium of absolute ether.   15 g of the bromo ketone in 25 ml of ether was added slowly and with constant stirring to 14 g of dry sodium ethoxide in 150 ml of absolute ether; the reaction mixture immediately acquired a yellow-orange color and heat evolution was observed when the solution was added rapidly. The red ethereal solution was separated by decantation after completion of the reaction, ether was drawn off under vacuum and the residue was distilled. 0.75 g of ethyl-lactolide of ethylbenzoylcarbinol was isolated in the form of a colorless readily mobile liquid with a pleasant fruity odor; b.p. 91-93° at 8 mm, $n^{20}D$ 1.4865.

Found %: C 74.86; H 8.35. M 193. $C_{12}H_{16}O_2$ Calculated %: C 75.0;   H 8.33. M 192.

The ethyl-lactolide is very unstable and rapidly changes in storage, this being accompanied by the development of a penetrating and unpleasant odor, increase of the index of refraction and decrease of the percentage content of the ethoxy group.

The solid residue which remained after the decantation of the ethereal solution was treated with water and an organic substance was extracted with ether from the solution. A distillation was run after drying with magnesium sulfate. 2.7 g of ethylbenzoylcarbinol was isolated.

Found %: C 72.83, 72.86;   H 7.55, 7.49. M 153. $C_{10}H_{12}O_2$ Calculated %: C 73.17; H 7.32. M 164.

3. Action of sodium ethoxide on α-bromobutyl phenyl ketone in alcoholic solution. a) Solution of 16 g of the bromo ketone in 10 ml of alcohol was added to a solution of sodium ethoxide (1.6 g of sodium and 40 ml of anhydrous alcohol). The precipitate of sodium bromide was separated from the solution by centrifuging after one hour; the alcohol was distilled off under vacuum with gentle heating. 1.8 g of ethyl-lactolide of propylbenzoylcarbinol was isolated after two distillations, the product being a mobile colorless liquid with a pleasant fruity odor; b.p. 98-100° at 8 mm, $n^{20}D$ 1.4931.

Found %: C 75.81, 75.66; H 9.02, 8.98. $C_{13}H_{18}O_2$ Calculated %: C 75.72; H 8.73.

Ethyl-lactolide of propylbenzoylcarbinol is very unstable; an unpleasant odor develops rapidly in storage, the index of refraction rises and the percentage content of the ethoxyl declines.

b) 15 g of the bromo ketones in 25 ml of alcohol was added to the solution of sodium ethoxide in anhydrous alcohol (2 g of sodium and 50 ml of alcohol). The mixture was heated at 40-50° until the test for halogen in the organic substance became negative (approximately ten hours). Carbon dioxide was passed into the reaction mixture, the precipitate of sodium bromide and sodium carbonate was centrifuged off and the residue was vacuum distilled. The main substance, boiling at 119-120.5° (4 mm) and being, according to the analyses for carbon, hydrogen, ethoxyl and hydroxyl groups and the percentage content of keto alcohol as determined by the Fehling solution, a mixture of ethyl-lactolide, diethyl ketal of propylbenzoylcarbinol and propyl α-ethoxybenzyl ketone, was isolated after two redistillations. The osazone of propylbenzoylcarbinol, in the form of shiny red crystals with m.p. 244-245°, was isolated by the hydrolysis of this mixture by heating with dilute sulfuric acid and a subsequent treatment of the hydrolysis product with excess 2,4-dinitrophenylhydrazine.

Found %: N 20.59, 20.57. $C_{23}H_{20}O_8N_8$. Calculated %: N 20.89.

c) The reaction and the treatment of the reaction products were run under the same conditions but the reaction mixture was heated for four hours. Since an evident decomposition of the substance, which was mainly the diethyl ketal of propylbenzoylcarbinol, occurred during its repeated distillations, the entire substance was heated under 3 mm vacuum for half an hour to the temperature of incipient boiling. The oxo alcohol was washed away from the ethereal solution with water. 2,4-Dinitrophenylhydrazine was added to the residue and propyl α-ethoxybenzyl ketone was isolated and characterized as the 2,4-dinitrophenylhydrazone; yellow needle-shaped crystals melting at 110-111°.

Found %: N 14.84, 14.54. $C_{19}H_{22}O_5N_4$. Calculated %: N 14.51.

4. Action of sodium ethoxide on α-bromobutyl phenyl ketone in the medium of absolute ether. 15 g of the bromo ketone in 25 ml of ether was added gradually and with constant stirring to 20 g of dry sodium ethoxide in 200 ml of absolute ether. The reaction was complete after ten hours; the solution was deep red. After the separation of sodium bromide and excess sodium tethoxide, the ether was drawn off under vacuum from the solution. 2 g of ethyl-lactolide of propylbenzoylcarbinol was isolated by distillation of the residue. The substance was similar in all its properties to the ethyl-lactolide isolated in experiment 3a.

5. Action of zinc chloride on ethyl-lactolide of propylbenzoylcarbinol. Several milliters of a saturated ethereal solution of anhydrous zinc chloride was added to 2 g of the ethyl-lactolide in 10 ml of absolute ether. An attempt was made to distil the reaction product under vacuum, but after having been heated to 100° (3 mm) the entire mass suddenly crystallized to fine colorless crystals. The substance had m.p. 215-217° (in a sealed capillary) after three recrystallizations from benzene.

Found %: C 75.65, 75.61; H 8.89, 8.91. M (after Rast.) 391. $C_{26}H_{30}O_4$. Calculated %: C 75.72; H 8.73. M 412.

Dimerization of the ethyl-lactolide with formation of cyclo-diethyldilactolide of propylbenzoylcarbinol occured during heating in the presence of zinc chloride.

SUMMARY

1. The first representatives of ethyl-lactolides of two secondary alkaromatic α-oxo alcohols – ethylbenzoylcarbinol and propylbenzoylcarbinol – were prepared. These ethyl-lactolides are considerably less stable than the methyl-lactolides of the same alcohols.

2. The corresponding ketals are obtained in the reaction of the ethyl-lactolides with ethyl alcohol. The diethyl ketals are poorly stable. The diethyl ketal of ethylbenzoylcarbinol is rapidly transformed into cyclo-diethyl-dilactolide of ethylbenzoylcarbinol in the cold in the pure state or on being heated in an alcoholic solution. Both diethyl ketals are transformed into ethyl ethers of the α-oxo alcohols containing the propionyl group during attempts to distill them under an insufficient vacuum.

3. Dimerization of ethyl-lactolide of propylbenzoylcarbinol into cyclo-diethyl-dilactolide takes place during the action of zinc chloride on the former.

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STUDIES IN THE FIELD OF AMINES AND AMMONIUM COMPOUNDS

XI. CONCERNING THE PROBLEM OF THE EFFECT OF THE CHARACTER OF NITROGEN AND OF THE STRUCTURE OF THE MOLECULES ON THE BOND STRENGTHS IN AMINES AND QUATERNARY AMMONIUM COMPOUNDS, CONTAINING A HALO ALKYL GROUP

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As reported earlier [1], we have been devoted to the study of tertiary amines and quaternary ammonium salts containing a polyhalo alkyl group, in order to clarify the effect of the character of the nitrogen and of the structure of the molecule on the bond strength in amines and quaternary ammonium compounds containing the halo alkyl group, and in order to extend further the dehydrochlorination–cleavage reaction [2] of quaternary ammonium salts for the synthesis of compounds with conjugated unsaturated bonds.

The present communication is devoted to the synthesis of 1-dimethylamino-3-chlorobutane (V), -3-chloro-3-butene (VII), -3,4-dichloro-3-butene (VIII), -2,3,3-trichlorobutane (X), -3,3,4-trichlorobutane (XI), -3,3,4,4-tetrachlorobutane (XII) and -3,4,4-trichloro-3-butene (XIII), to the reaction of these amines with alcoholic alkali and to the alkaline cleavage of the methiodides: (Va), (VIa), (VIIa), (VIIIa), (Xa), (XIa) and (XIIa).

The synthesis starting with dimethylamino-2-butyne was accomplished by the following scheme:
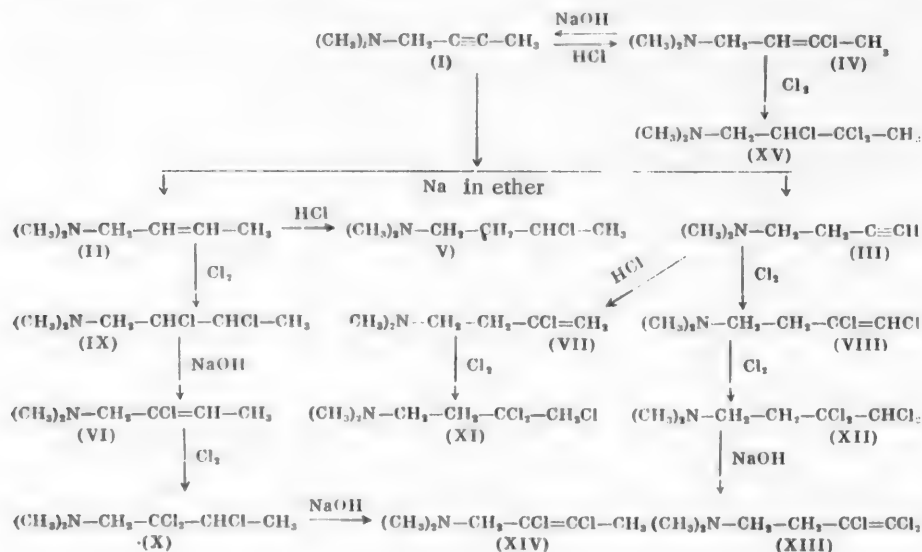
As it should have been expected [3], hydrochlorination of amine (II) leads to the formation of amine (V). We failed to find any literature indications concerning the order of addition of hydrogen chloride to dialkyl-

TABLE 1

Results of Hydrochlorination (Experiments 1–3), Chlorination (Experiments 4–7) and Dehydrochlorination (Experiments 8) of Amines

Expr. no.	Starting compound	Compound obtained	Yield (in %)	B. p. (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calc.	M. p. of derivatives hydrochloride	M. p. of derivatives picrate	M. p. of derivatives methiodide	Content of iodine in methiodide (in %) found	empirical formula	calc.	Remarks
1	(I)	(IV)	77.7	135—138° (680)	—	—	—	—	143°	120°	176°	—		—	[5]
2	(II)	(V)	98.0	38—39 (10)	0.9038	1.4315	39.11	38.71	168	151	178	—		—	[12]
3	(III)	(VII)	80.5	135—138 (680)	0.9279	1.4440	38.22	38.24	148	119	198	46.16	$C_7H_{15}NClI$	46.09	
4	(III)	(VIII)	80.0	60—65 (10)	1.0891	1.4688	42.93	43.14	187	145	214	40.50	$C_7H_{14}NCl_2I$	40.90	
5	(III)	(XII)	60.0	95—96 (19)	1.3106	1.4977	53.41	53.30	203	166	212	33.58	$C_7H_{14}NCl,I$	33.33	Forms much tar during distillation
6	(VI)	(X)	61.1	73—74 (10)	1.1986	1.4768	48.19	48.44	172	143	227	36.98	$C_7H_{15}NCl_3J$	36.65	
7	(VII)	(XI)	60.7	86—90 (11)	1.2110	1.4805	48.05	48.44	161	142	208	37.08	$C_7H_{15}NCl_3J$	36.65	Forms much tar during distillation
8	(XII)	(XIII)	70.0	69—71 (6)	1.2145	1.4880	48.03	47.98	205	136	221	36.46	$C_7H_{13}NCl_3J$	36.86	The dehydrochlorination was run at room temperature

aminoacetylenes. However, the data on hydration of dialkylaminoacetylenes [4] gave grounds to suppose that the hydrochlorination of amine (III), in which the triple bond is a terminal one, would proceed in accord with the Markovnikov rule and would lead to formation of amine (VII). In case of amine (I) the deciding influence would be the directing effect of the ammonium group and the hydrochlorination should lead to amine (IV).

The hydrochlorination was accomplished by passage of a stream of dry hydrogen chloride through the molten hydrochloride of the amine at 140-160°. It should be noted that the addition of a second molecule of hydrogen chloride does not occur under these conditions both in case of amine (I) and that of amine (III).

The results of the hydrochlorination fully justified our expectations (Table 1, No. 1-3). The structure of amine (VII) was proved by sulfuric acid hydrolysis which led to dimethylaminobutanone which was identical with 1-dimethylamino-3-butanone prepared as the result of a sulfuric acid hydrolysis of 1-dimethylamino-3-chloro-2-butene [5].

$$(VII) \xrightarrow{H_2SO_4} (CH_3)_2N-CH_2-CH_2-CO-CH_3 \xleftarrow{H_2SO_4} (IV)$$
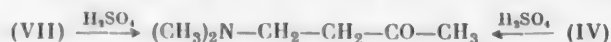
The chlorination of aqueous solutions of hydrochlorides shown in the amine scheme above proceeds smoothly and leads to the formation of products of chlorine addition at the site of the double bond [6]. It is possible to obtain a high yield of amine (VIII) by incomplete chlorination, owing to the sharp difference in the rates of addition of the first and the second pairs of chlorine atoms to amine (III). The product of complete chlorination of amine (III) may be also obtained in high yield, but this forms much tar during a distillation; for this reason, in the preparation of the methiodide the crude product was directly taken for the reaction with methyl iodide and the precipitated methiodide (XIIa) was purified by recrystallization. The results of the chlorination are given in Table 1 (No. 4-7).

In the determination of the relative rates of dehydrochlorination of the amines and of their methiodides, the reaction with alkali was run at room temperature; that with amines in alcoholic and that with the methiodides in an aqueous solution. The degree of dehydrochlorination was estimated by the amount of ionic chlorine formed. The resulting data are given in Table 2; it is clear from these data that the reaction of dehydrochlorination (if it does occur) is facilitated by the passage from the amine to its methiodide. The apparent inconsistency between the data from (VIII) and from (VIIIa) is explained by the disruptability of (VIIIa) in the alkaline medium as will be seen further. The results thus obtained clearly indicate also the dependence of the dehydrochlorination reaction on the structure.

Factors having a clearly displayed effect on the bond strength in the molecule (atoms of chlorine, amino group, double bonds) are present in the amines studied by us. In case of a coincidence of the effects of these factors on the dehydrochlorination reaction, the total effect should be naturally enhanced, while in the opposite case it should be weakened or could even bring about a change in the order of cleavage of hydrogen chloride. Such phenomena should be especially noticeable in transition from the amine to its methiodide. It was interesting, from this point of view, to study the order of cleavage of elements of hydrogen chloride from the amines and from their methiodides during their dehydrochlorination. Saturated amines and their methiodides were selected for the clarification of the total picture. The determination was run in the following manner: amines and their methiodides were subjected to dehydrochlorination. The methiodide of the dehydrochlorinated amine was prepared and, if this turned out to be identical with the dehydrochlorinated methiodide, this was considered to be the proof of the identity of the order of cleavage of elements of hydrogen chloride. The results obtained are given in Table 3. The results of the alkaline cleavage of the methiodides are given in Table 4. The data in Table 3 relative to compounds (V) and (Va), (IX) and (IXa), (XII) and (XIIa), (XV) and (XVa) indicate that the order of cleavage of hydrogen chloride among these compounds coincides for the amine and for its methiodide.

As it is known, the dehydrochlorination of 2,3-dichlorobutane proceeds in accord with the Zaitsev rule and leads to the formation of 2-chloro-2-butene, while dehydrochlorination of 1,2,3-trichlorobutane leads to a mixture of cis- and trans-isomers of 1,2-dichloro-2-butene [7]. Merely on the basis of the cited literature data as well as the results of dehydrochlorination of (V) and (Va), we were justified in expecting the formation of 2-chloro-2-butenyl radical in the dehydrochlorination of amine (IX) and its methiodide (IXa), along with an acceleration of the dehydrochlorination reaction in passage from the amine to its methiodide. Data given in Tables 2 and 3 confirm this. The reaction scheme is given below.

$$(CH_3)_2N-CH_2-CHCl-CHCl-CH_3$$
$$(IX)$$

CH₃I ↓   ↓ NaOH

$$(CH_3)_3\overset{+}{N}-CH_2-CHCl-CHCl-CH_3 \qquad\qquad (CH_3)_2N-CH_2-CCl=CH-CH_3$$
$$I^-$$
$$(IXa) \qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad (VI)$$

NaOH ↓   ↓ CH₃I

$$(CH_3)_3\overset{+}{N}-CH_2-CCl=CH-CH_3$$
$$I^-$$
$$(VIa)$$
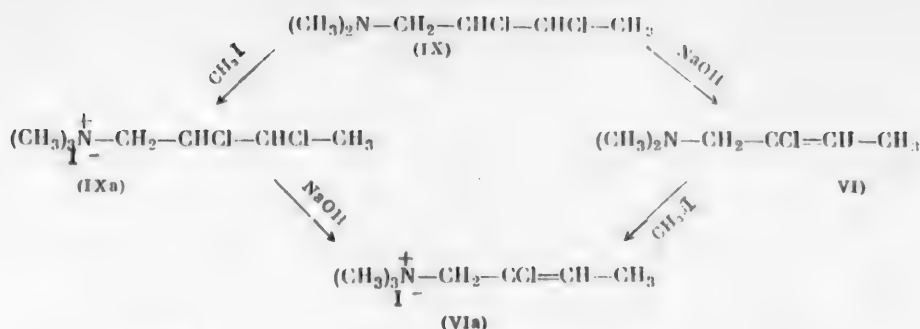
TABLE 2

Results of the Reaction of the Amines and Their Methiodides with Alkali at Room Temperature

Nature of R in the starting material	Duration of reaction (in hours)	Am't of resulting halide (g-atoms/mole of compound)	
		amine	methiodide
(V)—CH_2—CH_2—$CHCl$—CH_3	10	0.104	0.357
(VI)—CH_2—$CCl=CH$—CH_3	10	0.00	0.25
(VII)—CH_2—CH_2—$CCl=CH_2$	10	0.00	0.00
(VIII)—CH_2—CH_2—$CCl=CHCl$	10	0.82	0.52
(IX)—CH_2—$CHCl$—$CHCl$—CH_3	10	0.27	1.00
(X)—CH_2—CCl_2—$CHCl$—CH_3	10	0.6	2.58
(XI)—CH_2—CH_2—CCl_2—CH_2Cl	10	0.89	1.54
(XII)—CH_2—CH_2—CCl_2—$CHCl_2$	10	1.03	1.92
(XII)—CH_2—CH_2—CCl_2—$CHCl_2$	1	0.80	0.88*
(XV)—CH_2—$CHCl$—CCl_2—CH_3	4	0.886	0.88

* The dehydrochlorination of the amine and the methiodide was run by the action of an equimolar amount of alcoholic alkali of same concentration.

TABLE 3

Results of Dehydrochlorination of Amines and Their Methiodides

Value of R		M.p. of methiodide	Remarks
starting material	product obtained		
(V)—CH_2—CH_2—$CHCl$—CH_3 (Va)*	(II)—CH_2—$CH=CH$—CH_3 (IIa)*	151° 151	Mixed melting point of both methiodides gives no depression
(IX)—CH_2—$CHCl$—$CHCl$—CH_3 (IXa)*	(VI)—CH_2—$CCl=CH$—CH_3 (VIa)*	161—162 161—162	Mixed melting point gave no depression
(X)—CH_2—CCl_2—$CHCl$—CH_3 (Xa)*	(XIV)—CH_2—$CCl=CCl$—CH_3 Products of cleavage	225	
(XV)—CH_2—$CHCl$—CCl_2—CH_3 (XVa)*	(XIV)—CH_2—$CCl=CCl$—CH_3 Products of cleavage	225	
(XII)—CH_2—CH_2—CCl_2—$CHCl_2$ (XIIa)*	(XIII)—CH_2—CH_2—$CCl=CCl_2$ (XIIIa)*	220 220	Mixed melting point gave no depression

* Methiodide.

TABLE 4

Results of Alkaline Cleavage of Amine Methiodides

Value of R in starting material (methiodide)	Compound obtained	Yield (in %)	B. p. (in pressure)	d_4^{20}	n_D^{20}	% Cl found	% Cl calc.	Remarks
(V a) —CH₂—CH₂—CHCl—CH₃	CH₂=CH—CH=CH₂*	95	—	—	—	—	—	M.p. of tetrabromide 118°. Gives no depression in mixed m.p. with butadiene tetrabromide
(X a)—CH₂—CCl₂—CHCl—CH₃	CH₂=CCl—CCl=CH₂ CH₃—CH=CH—COOH**	34.2 51.5	90—93°(680) M.p. 70	1.1870 —	1.4899 —	57.01 —	57.72 —	[13] A liquid isomer is also formed
	HC≡C—C≡CH	—	—	—	—	—	—	M.p. of hexabromide 181° [14]
(XI a)—CH₂—CH₂—CCl₂—CH₂Cl	CH₂=CH—CCl=CHCl HC≡C—C≡CH	69.1 —	105—106(680) —	1.1551 —	1.5007 —	56.92 —	57.72 —	[15] Melting point of hexabromide 181° [14]
(XII a)—CH₂—CH₂—CCl₂—CHCl₂	CH₂=CH—CCl=CCl₂	70	45 (15)	1.4546	1.5402	67.72	67.61	1,1,2-Trichloro-1,3-butadiene described for the first time
(VI a)—CH₂—CCl=CH—CH₃	CH₂=CH—C≡CH	82	—	—	—	—	—	No chloroprene found among the reaction products
(VII a)—CH₂—CH₂—CCl=CH₂	CH₂=CH—CCl=CH₂	90	56—58 (680)	0.9535	1.4593	39.51	40.01	[16]
(VIII a)—CH₂—CH₂—CCl=CHCl	CH₂=CH—CCl=CHCl CH₂=CH—C≡CCl	42 46	101—102(680) 52—53 (680)	1.1803 1.0022	1.5009 1.4656	57.22 39.0	57.72 41.04	[15] Gives a yellow precipitate with the Ilosvay solution [17]

* Found %: Br in tetrabromide 84.93; calculated 85.51.

** Found % Ag in the salt 55.74; calculated 55.62.

The 2,3,3-trichlorobutyl radical is present in amine (XV). The dehydrochlorination of 2,3,3-trichloro-butane leads, as it is known, to a mixture of geometric isomers of 2,3-dichloro-2-butene [8]. It is not difficult to see that the formation of 2,3-dichloro-2-butenyl radical should be expected as the result of dehydrochlorina-tion of (XV). Amine (XV) indeed does form 1-dimethylamino-2,3-dichloro-2-butene during the dehydrochlor-ination, as may be seen among the data in Table 3. Unfortunately, owing to the exceptionally facile decom-position of the dehydrochlorinated methiodide in an alkaline medium, we failed to isolate this substance. Pro-ducts of its cleavage — trimethylamine and 2,3-dichloro-1,3-butadiene — were obtained instead of the expect-ed (XIVa). Part of the original methiodide was recovered unchanged. Alkaline cleavage of (XVa) leads to tri-methylamine and 2,3-dichloro-1,3-butadiene in an almost quantitative yield.

We succeeded in isolating the dehydrochlorinated methiodide by replacing (XVa) by methyldiethyl-(2,3,3-trichlorobutyl)-ammonium iodide and we showed that this was identical with 1-diethylamino-2,3-di-chloro-2-butene methiodide.
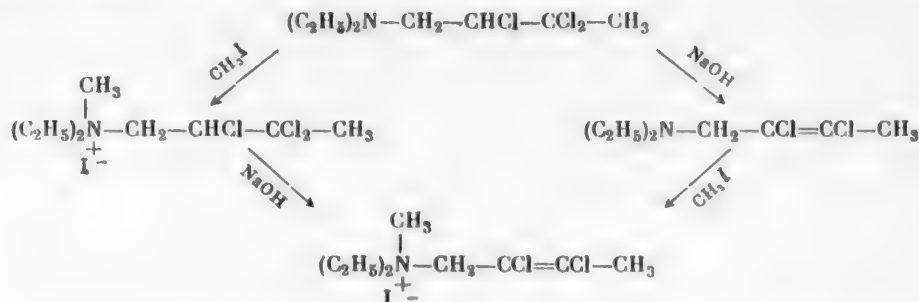
In compound (X) with the reverse disposition of chlorine atoms in comparison with (XV) one should ex-pect a repression of the rate of the dehydrochlorination reaction in the direction of formation of 2,3-dichloro-2-butenyl radial or even an alteration in the order of cleavage of hydrogen chloride, in comparison with (XV). The effect of the amino group in (X) is not so great as to alter the order of cleavage of the elements of hydro-gen chloride, as it is evident from the results of dehydrochlorination, but it clearly affects the reaction rate (Table 2).

We also failed to isolate the dehydrochlorination product from (Xa). Its reaction with alkali leads to the formation of 2,3-dichloro-1,3-butadiene and products of complete dehydrochlorination — cleavage, i.e., cro-tonic acid and a small amount of diacetylene (Table 4), which fact indicates the change of the order of cleavage of hydrogen chloride.

Thus, the effect of chlorine bound with the γ-carbon atom in amine (X) is stronger than the effect of the dimethylamino group bound with the α-carbon atom, and the dehydrochlorination proceeds at the hydrogen of the γ-carbon atom.

$$(CH_3)_2N-CH_2-CCl_2-CHCl-CH_3 \xrightarrow{NaOH} (CH_3)_2N-CH_2-CCl=CCl-CH_3$$
$$(X) \qquad\qquad\qquad (XIV)$$
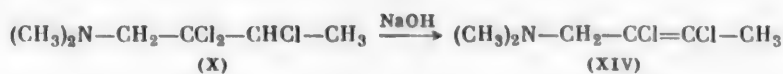
The effect of the ammonium group in methiodide (Xa) is already competing with the effect of γ-chlo-rine which fact leads to two parallel reactions in which the order of cleavage of hydrogen chloride differs from each other.

$$\xrightarrow{\text{(a)}} (CH_3)_3N + CH_2=CCl-CCl=CH_2$$

$$(b) \begin{cases} \longrightarrow (CH_3)_3\overset{+}{N}-C\equiv C-CH=CH_2 \quad \underset{I^-}{\xrightarrow{\text{NaOH}}} (CH_3)_3N + CH_3-CH=CH-COOH \\ \longrightarrow (CH_3)_3\overset{+}{N}-CH=C=C=CH_2 \quad \underset{I^-}{\xrightarrow{\text{NaOH}}} (CH_3)_3N + HC\equiv C-C\equiv CH \end{cases}$$
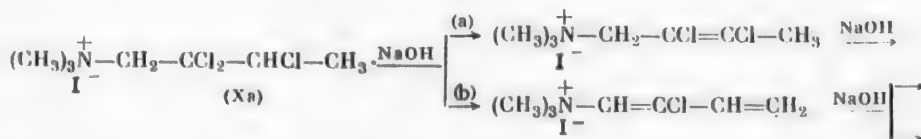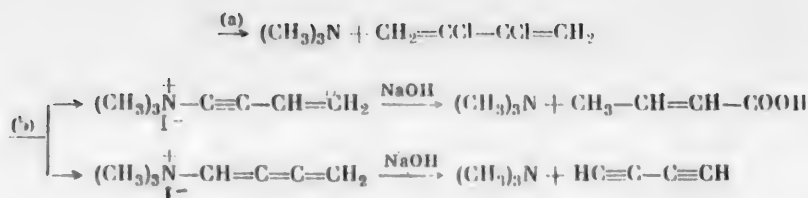
In reaction b) we have an analogy with the reaction of alkaline cleavage of trimethyl-2,2,3,3-tetrachloro-butylammonium iodide which leads to the formation of tetrolic acid [9]. The formation of 2.5 gram atoms of ionic chlorine per mole of methiodide used was shown to take place in the aqueous layer of the products of alkaline cleavage of methiodide (Xa). These data indicate that the ratio of the reaction products formed by b) with total dehydrochlorination and the reaction products formed by a) with cleavage of one molecule of hydrogen chloride should be about 3:1.

Reaction of amine (XII) with alcoholic alkali at room temperature leads to cleavage of one molecule of hydrogen chloride and to the formation of 1-dimethylamino-3,4,4-trichlorobutene whose methiodide is identical with the methiodide formed in the reaction of alcoholic solutions of equimolar amounts of methiodide (XIIa) and sodium hydroxide at room temperature. Consequently, the order of cleavage of hydrogen chloride from the amine and the methiodide is the same under these conditions. The following possibilities exist for the cleavage of the first molecule of hydrogen chloride:

$$(CH_3)_2N-CH_2-CH_2-CCl_2-CHCl_2 \xrightarrow{\text{NaOH}} \begin{cases} \overset{\text{(a)}}{\longrightarrow} (CH_3)_2N-CH_2-CH_2-CCl=CCl_2 \\ \overset{\text{(b)}}{\longrightarrow} (CH_3)_2N-CH_2-CH=CCl-CHCl_2 \end{cases}$$

$$(XII)$$
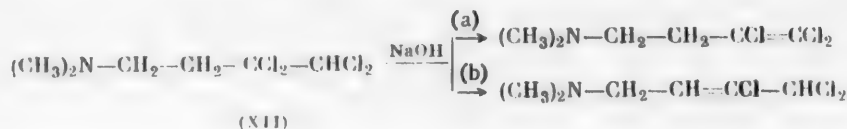
The dehydrochlorinated amine yields 1-dimethylamino-3-butyne on being treated with powdered metallic sodium [10]. We have not established firmly the location of the double bond in the 3,4,4-trichlorobutenyl radical; however, we regard, on the basis of the data cited above, that the reaction of dehydrochlorination of amine (XII) and methiodide (XIIa) proceeds at room temperature according to scheme a.

Alkaline cleavage of (XIIa) leads to trimethylamine (90%) and 1,1,2-trichloro-1,3-butadiene (70%). The formation of 1.9 gram atoms of ionic chlorine per mole of salt (XIIa) was discovered in the aqueous layer. This indicates that one should look for about 30% of products of complete dehydrochlorination – cleavage, in addition to 1,1,2-trichloro-1,3-butadiene. The possibility of formation of tetrolic acid is not excluded, but we have thus far failed to establish its presence among the reaction products. The alkaline cleavage of (XIIa) may be represented as proceeding by the following scheme:

$$(CH_3)_3\overset{+}{\underset{I^-}{N}}-CH_2-CH_2-CCl_2-CHCl_2 \xrightarrow{\text{NaOH}} \begin{cases} \overset{\text{(a)}}{\longrightarrow} (CH_3)_3\overset{+}{\underset{I^-}{N}}-CH_2-CH_2-CCl=CCl_2 \xrightarrow{\text{NaOH}} \\ \overset{\text{(b)}}{\longrightarrow} (CH_3)_3\overset{+}{\underset{I^-}{N}}-CH_2-CH=CCl-CHCl_2 \xrightarrow{\text{NaOH}} \begin{cases} \overset{\text{(c)}}{\longrightarrow} \\ \overset{\text{(d)}}{\longrightarrow} \end{cases} \end{cases}$$

$$(XIIa)$$

$$\xrightarrow{\text{NaOH}} (CH_3)_3N + CH_2=CH-CCl=CCl_2$$

$$\xrightarrow{\text{NaOH}} \begin{cases} \overset{\text{(c)}}{\longrightarrow} (CH_3)_3N + CH_2=CH-CCl=CCl_2 \dots 1,4 \text{ cleavage} \\ \overset{\text{(d)}}{\longrightarrow} (CH_3)_3\overset{+}{\underset{I^-}{N}}-CH=CH-CCl=CHCl \dots 1,4 \text{ dehydrochlorination} \end{cases}$$
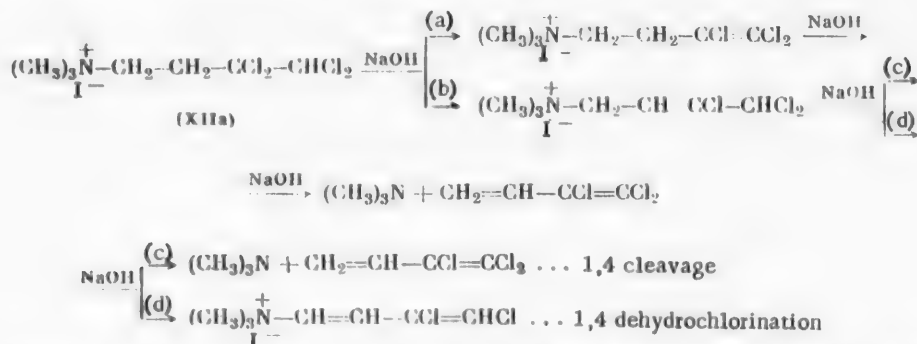
Formation of 1,1,2-trichloro-1,3-butadiene may proceed, as it is evident from the above scheme both in direction (a) and in direction (b). Reaction (c) continues further, leading to the products of total dehydrochlorination–cleavage. The study of the reaction is being continued.

We have thus far failed to isolate and identify the dehydrochlorination products of amines (VIII) and (XI) and for this reason we cite only the results of alkaline cleavage of their methiodides. Alkaline cleavage of

methiodide (VIIIa) leads to the formation of trimethylamine (90%), 1,2-dichloro-1,3-butadiene (41%) and vinyl-ethynyl chloride (46%). In accord with these results we showed the formation of 0.51 gram atoms of ionic chlorine per mole of the methiodide (VIIIa) used for the reaction in the aqueous layer. The reaction proceeds by the following scheme:

$$(CH_3)_3\overset{+}{N}-CH_2-CH_2-CCl=CHCl \quad \overset{NaOH}{\underset{I^-}{}} \quad \begin{array}{l} \overset{(a)}{\longrightarrow} (CH_3)_3N + CH_2=CH-CCl=CHCl \\ \overset{(b)}{\longrightarrow} (CH_3)_3\overset{+}{\underset{I^-}{N}}-CH_2-CH_2-C\equiv CCl \xrightarrow{NaOH} \end{array}$$

(VIIIa)

$$\xrightarrow{NaOH} (CH_3)_3N + CH_2=CH-C\equiv CCl$$
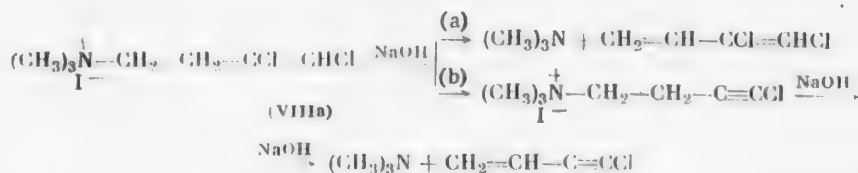
The yield of nonnitrogenous cleavage products, as well as the amount of ionic chlorine formed, indicate that the two parallel reactions: the cleavage (a) and dehydrochlorination–cleavage (b) proceed at the same rate. Cleavage of (VIIIa) by aqueous alkali resembles the cleavage of ammonium salts containing the 3-chloro-2-butenyl radical which leads to the formation of both cleavage products (chloroprene) and those of dehydrochlorination–cleavage (vinylacetylene) [2].

One may expect results of alkaline cleavage of methiodide (XIa) which would be similar to the results of alkaline cleavage of (VIIIa). However, 1,2-dichloro-1,3-butadiene (70%) and a small amount of diacetylene, identified through its hexabromide, were obtained from the alkaline cleavage of (XIa). The absence of vinyl-ethynyl chloride among the reaction products indicates that the formation of 1,2-dichloro-1,3-butadiene does not proceed through a preliminary formation of (VIIIa). Formation of 1.54 gram atoms of ionic chlorine per mole of (XIa) taken for the reaction was shown in the aqueous layer. This indicates that over 25% of the methiodide was subjected to a total dehydrochlorination. It is quite possible that the reaction of (XIa) with aqueous alkali may proceed by scheme:

$$(CH_3)_3\overset{+}{\underset{I^-}{N}}-CH_2-CH_2-CCl_2-CH_2Cl \xrightarrow{NaOH} (CH_3)_3\overset{+}{\underset{I^-}{N}}-CH_2-CH=CCl-CH_2Cl \xrightarrow{NaOH} \begin{array}{l} \overset{(a)}{\longrightarrow} \\ \overset{(b)}{\longrightarrow} \end{array}$$

(XIa)

$$\overset{(a)}{\longrightarrow} (CH_3)_3N + CH_2=CH-CCl=CHCl \quad \ldots \quad 1,4\text{-cleavage}$$

$$\overset{(b)}{\longrightarrow} (CH_3)_3\overset{+}{\underset{I^-}{N}}-CH=CH-CCl=CH_2 \xrightarrow{NaOH} (CH_3)_3\overset{+}{\underset{I^-}{N}}-CH=CH-C\equiv CH \xrightarrow{NaOH}$$

$$\longrightarrow (CH_3)_3N + HC\equiv C-C\equiv CH.$$
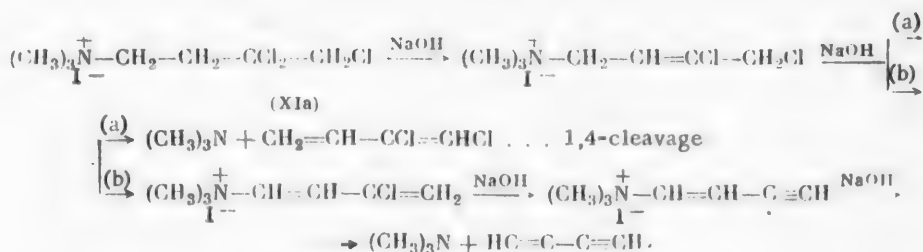
The possibility is not excluded that dehydrochlorination does not precede the cleavage in this reaction during the formation of 1,2-dichloro-1,3-butadiene, but occurs simultaneously with it or even follows it. Amine (VII), formed as the result of hydrochlorination of amine (III), turned out to be stable to alcoholic alkali at room temperature. The dehydrochlorination was accomplished by a four-hour refluxing with alcoholic alkali. It has been shown previously [11] that the presence of the dialkylamino group greatly facilitates both the isomerization of the disubstituted acetylenes into the monosubstituted ones under the influence of metallic sodium and the reverse isomerization into the disubstituted acetylenes under the influence of alcoholic alkali. Therefore, one should have expected the formation of dimethylamino-2-butyne as the result of dehydrochlorination of amine (VII) with alcoholic alkali; this was confirmed.

$$(CH_3)_2N-CH_2-CH_2-CCl=CH_2 \xrightarrow{NaOH} (CH_3)_2N-CH_2-C\equiv C-CH_3.$$

The alkaline cleavage of methiodide (VIIa) proceeds without dehydrochlorination and leads to the formation of trimethylamine and chloroprene. No ionic chlorine was found in the aqueous layer, in accord with this.

EXPERIMENTAL

The starting amines (II) and (III) were prepared from dimethylamino-2-butyne (I) by reaction with metallic sodium in an ethereal medium [11].

Hydrochlorination (Table 1, No. 1-3). A stream of dry hydrogen chloride was passed through the molten hydrochloride of the amine at 140-160° until this was completely saturated. Then the mixture was neutralized, made alkaline and the amine was extracted with ether.

Sulfuric acid hydrolysis of amine (VII). 25 ml of concentrated sulfuric acid was added, with cooling by means of ice water, to 5 g of the amine. The reaction mixture was neutralized after three days, extracted with ether and the extract was dried and distilled. 3 g (70%) of a liquid with b.p. 140-142° (680 mm) was obtained; picrate m.p. 108°. Mixed melting point with the picrate of 1-dimethylamino-3-butanone gave no depression.

Chlorination (Table 1, No. 4-7). Chlorine was passed through the solution of the amine in concentrated hydrochloric acid with water cooling until the absorption ceased. Then the mixture was neutralized with potassium carbonate, made alkaline with sodium hydroxide if necessary, the amine was extracted with ether, dried over anhydrous magnesium sulfate and distilled. Amines (XI) and (XII) were also isolated in the form of the hydrochlorides or methiodides owing to their facile tarring up. In the first case, the reaction mixture was concentrated to a small volume after the completion of passage of chlorine, alcohol was then added and the hydrochloride was precipitated with ether. Yield: 90-95%. In the second case, a solution of methyl iodide in acetone was added to the ethereal extract of the amine; the precipitated methiodide was purified by recrystallization. Yield: 85-90%.

Reaction of amines with alcoholic alkali and that of methiodides with aqueous alkali at room temperature. A solution of 0.005 mole of the substance being tested in 20 ml of 10% solution of sodium hydroxide was set aside at room temperature. Then the amount of ionic chlorine was determined by precipitation with silver nitrate. The amounts of the resulting ionic chlorine in gram atoms per mole of the compound are shown in Table 2.

Dehydrochlorination of amines (Table 3). The amine being tested was heated on a steam bath in a 25% sodium hydroxide solution in methyl alcohol. The resulting precipitate of sodium chloride was filtered off, washed with alcohol, dried and weighed (yield: 90-95%). The filtrate was diluted with water. The amine was extracted with ether, dried and distilled, after the solvent had been distilled off. The methiodide of the resulting amine was prepared. The mixed melting point with the methiodide prepared by dehydrochlorination of the methiodide of the original amine gave no depression.

Dehydrochlorination of methiodides. (Table 3). An alcoholic solution of 0.005 mole of the methiodide being tested and 0.005 mole of a standardized sodium hydroxide solution were set aside at room temperature. The precipitated sodium chloride was separated by filtration. Mixed melting point with the methiodide of the dehydrochlorination product of the corresponding amine showed no depression. The yield of dehydrochlorinated methiodide in cases of methiodides (Va), (IXa) and (XIIa) was nearly quantitative.

Dehydrochlorination of 1-dimethylamino-3,3,4,4-tetrachlorobutane. A solution of 23.9 g of the amine (XII) and 16 g of sodium hydroxide in 80 ml of methyl alcohol was set aside at room temperature. The reaction mixture was filtered from the precipitated sodium chloride after eight hours. The filtrate was diluted with water and extracted with ether. 14.2 g (70%) of amine (XIII) was isolated. The data are given in Table 1, No. 8. 10 g of the resulting amine was taken for the reaction with 5 g of powdered metallic sodium in 50 ml of absolute ether according to directions [10]. 3 g (60%) of amine with b.p. 98-104° was obtained after the hydrolysis and extraction with ether, the methiodide of this amine melting at 227° and giving no depression in mixed melting point with the 1-dimethylamino-3-butyne methiodide.

Preparation of 1-diethylamino-2,3,3-trichlorobutane. Theoretical amount of chlorine was passed into the solution of 161.5 g of 1-diethylamino-3-chloro-2-butene in 200 ml of concentrated hydrochloric acid with water cooling. 175 g (75.2%) of product was isolated after the usual treatment.

B.p. 100° at 6 mm, d^{20}_4 1.1512, n^{20}D 1.4781, MR_D 57.18; Calculated, 57.68
Found %: Cl 45.08. $C_8H_{16}NCl_3$. Calculated %: Cl 45.80

Methyldiethyl-(2,3,3-trichlorobutyl)-ammonium iodide. A mixture of 23.3 g of 1-diethylamino-2,3,3-trichlorobutane, 20 g of methyl iodide and 30 ml of acetone was heated for four hours on a water bath. The precipitated crystals melted at 187° after recrystallization from alcohol.

Found %: I 33.59. $C_9H_{19}NCl_3I$. Calculated %: I 33.91.

Dehydrochlorination of 1-diethylamino-2,3,3-trichlorobutane. A solution of 23.2 g of the substance, 16 g of sodium hydroxide and 60 ml of methyl alcohol was heated for seven hours on a steam bath. Theoretical amount of sodium chloride precipitated. The reaction mixture was diluted with water and extracted with ether. 14 g (80%) of 1-diethylamino-2,3-dichloro-2-butene was isolated.

B.p. 71-73° at 6 mm, d^{20}_4 1.0588, n^{20}_D 1.4760, MR_D 52.34. We failed to obtain a crystalline methiodide. Found %: I 38.15. $C_9H_{19}NCl_2I$. Calculated %: I 37.60.

An alcoholic solution of sodium hydroxide was added to a solution of methyldiethyl-(2,3-dichloro-2-butenyl)-ammonium iodide in methyl alcohol. The liquid was decanted from the sodium chloride precipitate and an alcoholic solution of picric acid was added to the solution. A picrate with m.p. 268-269° was isolated by evaporation of the alcohol to a small volume.

Dehydrochlorination of methyldiethyl-(2,3,3-trichlorobutyl)-ammonium iodide. 0.03 mole of standardized alcoholic sodium hydroxide solution was added to a solution of 0.03 mole of the substance in methyl alcohol, with water cooling. The precipitated sodium chloride (1.7 g) was filtered off and the filtrate was evaporated. 9.1 g (90%) of the methiodide was isolated. Picrate, m.p. 269°. Mixed melting point with the picrate obtained from the methiodide derivative of 1-diethylamino-2,3-dichloro-2-butene showed no depression.

Alkaline cleavage of methiodides (Table 4). 20-25% aqueous alkali was gradually added to the quaternary salt which was being heated on a water bath and stirred. The low-boiling reaction products were removed as formed from the reaction mixture. Trimethylamine was absorbed by a standarized acid solution. The volatile nonnitrogenous reaction products were collected either in a gasometer or in a cooled trap. Crotonic acid (cleavage of (Xa)) was extracted from the acidified reaction mixture with ether. Crystals with m.p. 70° gave no depression in a mixed melting point with an authentically prepared crotonic acid. The readily water soluble liquid isomer of crotonic acid was distilled from the acidified layer by means of steam and was identified by analysis of its silver salt. A higher temperature (110-115°) was required for cleavage of (Va).

SUMMARY

It was shown that hydrochlorination of a monosubstituted dialkylaminoacetylene occurs in accord with the Markovnikov rule. Hydrochlorination of a disubstituted dialkylaminoacetylene leads, under the influence of the ammonium group, to a compound with the chlorine that is at the carbon atom most remote from nitrogen.

The generality of the dehydrochlorination–cleavage reaction of halogen-containing quaternary ammonium salts with aqueous alkali was confirmed by new examples and the possibilities of its useful utilization in the syntheses of compounds with conjugated double bonds were shown.

Rules about the rates and the order of cleavage of hydrogen chloride being dependent on the character of the nitrogen and on the structure of the haloalkyl group bond to it were established.

1-Dimethylamino-3-chloro-3-butene, -3,4-dichloro-3-butene, -2,2,3-trichlorobutane, -3,3,4-trichlorobutane, -3,3,4-trichloro-3-butene, -3,3,4,4-tetrachlorobutane, 1-diethylamino-2,3,3-trichlorobutane, -2,3-dichloro-2-butene and 1,1,2-trichloro-1,3-butadiene were described for the first time.

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δ-LACTONES

XIII. SYNTHESIS OF 6-METHYL-5-ALKYL-3,4-DIHYDRO-α-PYRONES

N. P. Shusherina, R. Ya. Levina and Z. S. Sidenko

A new path for the synthesis of unsaturated δ-lactones (δ-enol lactones), consisting of monocyanoethylation of ketones, hydrolysis of the resulting nitriles into δ-oxo acids and lactonization of the latter, was described in our previous papers. δ-Enol lactones of various structures were prepared by this method: those with a condensed system of two and three rings (5,6-cycloalkano-3,4-dihydro-α-pyrones) [1-3], with the semicyclic location of the double bond (5-alkyl-6-alkylidenetetrahydro-α-pyrones) [4] and the lowest members of the series of mono- and dialkyl-3,4-dihydro-α-pyrones (6-methyl- and 5,6-dimethyl-3,4-dihydro-α-pyrones) [2, 5].

The previously undescribed 6-methyl-5-alkyl-3,4-dihydro-α-pyrones: 6-methyl-5-ethyl- (VII), 6-methyl-5-propyl- (VIII) and 6-methyl-5-butyl-3,4-dihydro-α-pyrones,(IX) were prepared in the present investigation by the use of this method.

$R = (I, IV, VII) C_2H_5; (II, V, VIII) C_3H_7; (III, VI, IX) C_4H_9.$
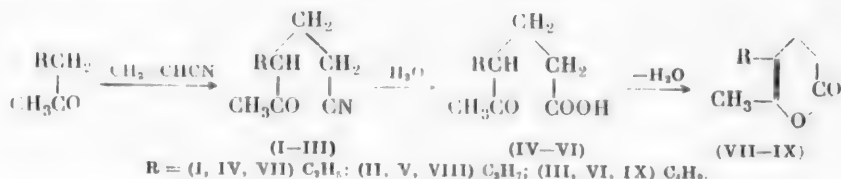
The starting ketones (methyl propyl, methyl butyl and methyl amyl ketones) were cyanoethylated under conditions used by us previously for cyanoethylation of methyl ethyl ketone [5]. γ-Acetylcapronitrile (I) and γ-acetylcaprylonitrile (III) (monocyanoethylated methyl propyl and methyl amyl ketones) were prepared by us in higher yields (41% and 50%) than indicated in the literature (14% and 18%, respectively). Monocyanoethylation of methyl butyl ketone has not been described in the literature.

Hydrolysis of the resulting nitriles (by heating with dilute hydrochloric acid [5]) led to the preparation of γ-acetylcaproic, γ-acetylenantic and γ-acetylcaprylic acids in yields of 96%, 93% and 91%, respectively. Unsaturated δ-lactones: 6-methyl-5-ethyl-[(VII), yield 60%], 6-methyl-5-propyl-[(VIII), yield 92%], and 6-methyl-5-butyl-3,4-dihydropyrones [(IX), yield 82%], were prepared by heating the above δ-oxo acids with acetyl chloride or acetic anhydride. The dialkyldihydro-α-pyrones readily opened their lactone ring under the influence of alcohol (in the presence of hydrogen chloride) and aqueous ammonia solution, forming esters (X, XI, XII) or amides (XIII, XIV, XV) of δ-oxo acids, respectively.

$R = (X \& XIII) C_2H_5; (XI \& XIV) C_3H_7; (XII \& XV) C_4H_9.$
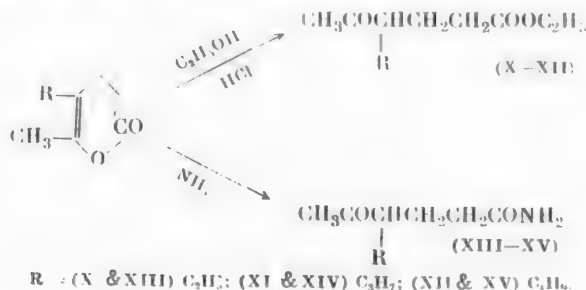
No. of compound	Name	B.p. (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calc.	Found (in %) C	Found (in %) H	Empirical formula	Calc. (in %) C	Calc. (in %) H	Yield (in %)
(VII)	6-Methyl-5-ethyl-3,4-dihydro-α-pyrone	94—96° (8)	1.4667	1.0347	38.13	37.90	68.40, 68.16	8.81, 8.89	$C_8H_{12}O_2$	68.57	8.56	94
(VIII)	6-Methyl-5-propyl-3,4-dihydro-α-pyrone	84—85 (3)	1.4684	1.0054	42.74	42.63	69.83, 69.72	8.95, 9.10	$C_9H_{14}O_2$	70.13	9.09	92
(IX)	6-Methyl-5-butyl-3,4-dihydro-α-pyrone	126—127 (10) 97—88 (3)	1.4673	0.9894	47.36	47.17	70.96, 71.01	9.64, 9.78	$C_{10}H_{16}O_2$	71.42	9.52	82

The resulting amides lost a molecule of water during standing for several days and were transformed into unsaturated lactams (XVI, XVII and XVIII).

$$R = (XVI)\ C_2H_5;\ (XVII)\ C_3H_7;\ (XVIII)\ C_4H_9.$$
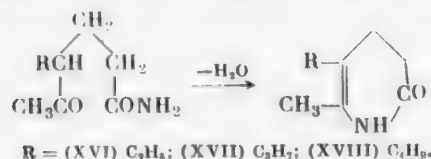
The ease of dehydration of the amides of δ-oxo acids (with formation of unsaturated lactams) calls for the supposition of the existence of a ring-chain tautomerism in them, tautomerism under which the amides of the δ-oxo acids may react in either the amide or the hydroxylactam forms [6, 7]:
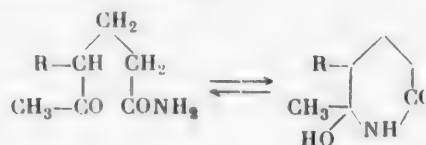
EXPERIMENTAL

Preparation of monocyanoethylated ketones (δ-oxo nitriles). To a mixture of 1 mole of the ketone[*] and 1.5 ml of 30% potassium hydroxide solution in methyl alcohol we added gradually with good stirring 0.20 mole of acrylonitrile at such a rate that the temperature of the reaction mixture did not rise above 25-30°. The reaction mixture was stirred for two hours at room temperature and was neutralized with concentrated hydrochloric acid; 3-5 ml of water was added for dissolution of the resulting potassium chloride. The upper layer was separated, dried with magnesium sulfate, the excess ketone was distilled from it and the residue was vacuum distilled. The resulting δ-oxo nitriles had the following constants after a redistillation.

γ-Acetylcapronitrile (I, yield 41%): b.p. 115-116° at 10 mm, n_D^{20} 1.4409, d_4^{20} 0.9482, MR_D 38.92. $C_8H_{13}ON$. Calculated 38.68.

According to data from [8]: b.p. 67° at 0.2 mm, n_D^{20} 1.4365 and 115-116° at 5 mm, n_D^{20} 1.4381, d_4^{20} 0.9624 [9].

γ-Acetylenantonitrile (II, yield 49%; undescribed in the literature): b.p. 109-110° at 7 mm, 147-149°

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[*] For prolonged storage of the ketone it is recommended that it be washed with a 2N sodium carbonate solution or that it be distilled before being used for the cyanoethylation reaction.

at 18 mm, n^{20}D 1.4409, d^{20}_4 0.9307, MR_D 43.51; calc. 43.51. $C_9H_{15}ON$. Calculated 43.54.

Found %: C 70.54, 70.60; H 10.11, 10.06. $C_9H_{15}ON$. Calculated %: C 70.58; H 9.80.

γ-Acetylcaprylonitrile (III, yield 60%): b.p. 148-149° at 18 mm, 158-159° at 28 mm, n^{20}D 1.4425, d^{20}_4 0.9222, MR_D 48.16. $C_{10}H_{17}ON$. Calculated 47.99. According to data from [10]: b.p. 124-26° (6 mm).

Preparation of δ-oxo acids. γ-Acetylcaproic acid (IV). A mixture of 70 g of γ-acetocapronitrile and 420 ml of dilute (2:1) hydrochloric acid was refluxed for six hours; the reaction mixture was diluted with one volume of water and was extracted for eight hours with ether, in a liquid-liquid extractor. Yield: 96%.

B.p. 151-152° at 5 mm, n^{20}D 1.4500, d^{20}_4 1.0449, MR_D 40.69. $C_8H_{14}O_3$. Calculated 40.67. According to data from [11]: b.p. 173-174° at 10 mm and 156-158° at 10 mm [10].

γ-Acetylenantic acid (V). A mixture of 70 g of γ-acetylenantonitrile and 420 ml of dilute (2:1) hydrochloric acid was refluxed for eight hours. The separated reaction product was combined with the ethereal extracts of the aqueous layer and was dried with sodium sulfate; γ-acetylenantic acid (64 g, yield: 91%) was isolated after the distillation of the ether; the acid had the following constants:

B.p. 138-139° at 4 mm, n^{20}D 1.4530, d^{20}_4 1.0210, MR_D 45.30. $C_9H_{16}O_3$. Calculated 45.54.

γ-Acetylcaprylic acid (VI) was prepared in 93% yield by the same method as was γ-acetylenantic acid.

B.p. 165-167° at 6 mm, n^{20}D 1.4504, d^{20}_4 1.0059, MR_D 49.92. $C_{10}H_{18}O_3$. Calculated 49.83. According to data from [10]: b.p. 150-151° at 2.5 mm.

Preparation of 6-methyl-5-alkyl-3,4-dihydro-α-pyrones. A mixture of 50 g of δ-oxo acid and 250 ml of acetyl chloride (or acetic anhydride was refluxed for five hours. After the acetyl chloride (or acetic anhydride) excess had been distilled off, the resulting lactones were vacuum distilled. The constants, the analytical data and the yields of the resulting δ-lactones (VII-IX) are given in Table 1.

Alcoholysis of 6-methyl-5-alkyl-3,4-dihydro-α-pyrones. A solution of 5 g of the lactone (VII-IX) in 50 ml of anhydrous alcohol was saturated with hydrogen chloride; the reaction mixture was poured into water and was extracted with ether. The constants and the yields of the resulting ethyl esters (X-XII) are given in Table 2.

TABLE 2

No. of compound	Name and empirical formula	B. p. (pressure in mm)	n_D	d	MR_D found	MR_D calc.	Yield (in %)
(X)	Ethyl γ-acetylcapoate $C_{10}H_{18}O_3$	101-102 (5)	1.4335	0.9879	49.78	50.04	62
(XI)	Ethyl γ-acetylenantate $C_{11}H_{20}O_3$	112-113 (6)	1.4360	0.9618	54.66	54.41	66
(XII)	Ethyl γ-acetylcaprylate $C_{12}H_{22}O_3$	110-111 (5)	1.4400	0.9552	59.07	59.28	60

Ammonolysis of 6-methyl-5-alkyl-3,4-dihydro-α-pyrones. Lactones (VII-IX) were dissolved in excess concentrated ammonium hydroxide (1:5) with stirring and very gentle heating. Crystals of the amide precipitated from the reaction mixture after evaporation of excess ammonia. The melting points (determined directly after recrystallization) and the yields of the amides prepared in this way (XIII-XV) are given in Table 3. These amides lost a molecule of water spontaneously on standing* and were transformed into the corresponding lactams (XVI-XVIII), whose melting points and analyses are given in Table 3.

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*The transformation of the amides into the lactams may be accelerated by their being distilled under vacuum.

TABLE 3

No. of compound	Amides — Name and empirical formula	Yield (in %)	M.p.	No. of compound	Lactams — Name	M.p.	Found (in %) C	H	Empirical formula	Calc. (in %) C	H
(XIII)	γ-Acetylcaproamide C₉H₁₅O₂N	60	105—106° (from ether)	(XVI)	6-Methyl-5-ethyl-3,4-dihydro-α-pyridone	87—88° (from water)	68.70, 68.62	9.05	$C_8H_{13}ON$	69.06	9.35
(XIV)	γ-Acetylenantamide $C_9H_{17}O_2N$*	92	123—125 (from aqueous alcohol)	(XVII)	6-Methyl-5-propyl-3,4-dihydro-α-pyridone	68—70 (from ether)	70.37, 70.60	9.94, 9.90	$C_9H_{15}ON$	70.58	9.85
(XV)	γ-Acetylcaprylamide $C_{10}H_{19}O_2N$	90	114—115 (from aqueous alcohol)	(XVIII)	6-Methyl-5-butyl-3,4-dihydro-α-pyridone	57—58 (from petroléum ether)	71.28, 71.23	10.10, 10.15	$C_{10}H_{17}ON$	71.85	10.18

*Found %: C 63.34, 63.26; H 10.08, 10.14. $C_9H_{17}O_2N$. Calculated %: C 63.10; H 10.00. Amides (XIII) and (XV) could not be analyzed owing to their rapid transformation into the lactams.

SUMMARY

The previously undescribed 6-methyl-5-alkyl-3,4-dihydro-α-pyrones: 6-methyl-5-ethyl-, 6-methyl-5-propyl- and 6-methyl-5-butyl-3,4-dihydro-α-pyrones, were synthesized from monocyanoethylated ketones by the method developed by us previously.

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δ-LACTONES

XIV. SYNTHESIS OF 6-METHYL-5-ALKYL-α-PYRONES

N. P. Shusherina, R. Ya. Levina, Z. S. Sidenko and
M. Yu. Lur'e

It has been established by us earlier that α-pyrones are formed in the distillation of 5,6-dibromo substituted bi- and tri-cyclic δ-lactones (prepared by bromination of δ- enol lactones condensed at 5,6-positions with polymethylene rings) [1, 2] as for example:
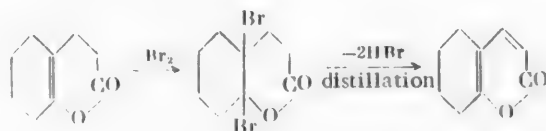
This path was used in the present work for the synthesis of 5,6-dialkyl-α-pyrones. It was shown that upon distillation of 5,6-dibromo-6-methyl-5-alkyltetrahydro-α-pyrones (V-VIII), prepared by bromination of 6-methyl-5-alkyl-3,4-dihydro-α-pyrones (I-IV) * [3], the corresponding α-pyrones are formed in yields of 10-17%; the low yield is caused by the circumstance that debromination occurs along with the dehydrobromination of the dibromides (V-VIII) [4], this leading to the formation of the original unsaturated δ-lactones (I-IV) (50-60%).
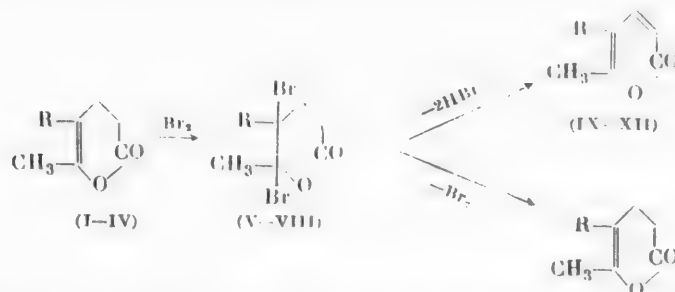
R = (I, V, IX) CH₃; (II, VI, X) C₂H₅; (III, VII, XI) C₃H₇; (IV, VIII, XII) C₄H₉.

The yield of α-pyrones rises to 25-46% if the dibromo lactones are heated under vacuum to 130-140° for 4-6 hours, after which they are distilled; the unsaturated δ-lactones and 5,6-dialkyl-α-pyrones may be readily isolated from the distillates by a fractional distillation through a column (the crystalline, 5,6-dimethyl-α-pyrone (IX) is, however, separated from the unsaturated lactone (I) by the process of freezing out). The

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* The 6-methyl-5-alkyl-3,4-dihydro-α-pyrones are readily prepared by a three step synthesis: cyanoethylation of methyl alkyl ketones, hydrolysis of the monocyanoethyl derivatives and subsequent lactonization of the resulting δ-oxo acids [3, 7].

difficultly accessible and previously undescribed 5,6-dialkylated α-pyrones: 5,6-dimethyl-[(IX), yield 27%] 6-methyl-5-ethyl-[(X), yield 25%], 6-methyl-5-propyl- [(XI), yield 38%] and 6-methyl-5-butyl-α-pyrone [(XII), yield 46%] were obtained by this method.

Thus, the cleavage of hydrogen bromide (by the preliminary heating and distillation) from dibromides of 6-methyl-5-alkyl-3,4-dihydro-α-pyrones may serve as a new general method of synthesis of 6-methyl-5-alkyl-α-pyrones.

The resulting 5,6-dialkyl-α-pyrones (except for the crystalline (IX), R = CH₃) possess a considerable exaltation of the molar refraction which is characteristic of compounds of the α-pyrone series [5].

The dialkylpyrones readily formed (in 80-85% yields) crystalline adducts (XIII-XVI) on being heated with maleic anhydride in xylene solution; the reaction was accompanied by evolution of nearly theoretical amount of carbon dioxide which indicated the formation of double adducts characteristic of α-pyrones [6] (two molecules of maleic anhydride per molecule of α-pyrone).*

R=(XIII) CH₃,(XIV) C₂H₅,(XV) C₃H₇,(XVI) C₄H₉.   R = (XVII) CH₃,(XVIII) C₃H₇,(XIX) C₄H₉.
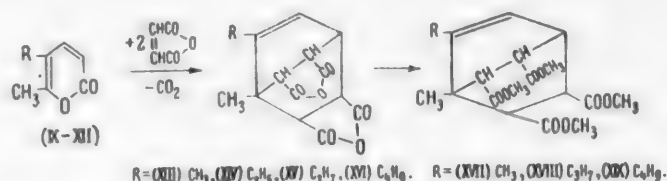
Adducts (XIII-XVI) were transformed into the corresponding tetrabasic acids by hydrolysis, and from these their tetramethyl esters (XVII-XIX) were prepared by the action of ethereal solution of diazomethane.

EXPERIMENTAL

<u>Preparation of dibromolactones (V-VIII).</u> 0.24 mole of dry bromine was added dropwise with stirring and cooling with salt-ice to a solution of 0.24 mole of δ-enol lactone (I-IV) [3, 7] in 25 ml of absolute ether; the ether was evaporated under vacuum in a stream of dry air. The resulting dibromides, which were viscous poorly mobile liquids (except for the crystalline V), which fumed strongly in air, were then subjected to a distillation or heating with a subsequent distillation in order to prepare the α-pyrones.**

<u>Preparation of 5,6-dimethyl-α-pyrone (IX).</u> Dibromolactone (V) (29 g, m.p. 63°) was slowly distilled under vacuum in a stream of dry air. The distillate obtained after a redistillation (8.5 g, b.p. 95-120° at 8-10 mm, n_D^{20} 1.4920) was subjected to freezing out;*** 3.2 g of a substance with m.p. 62-63° (from gasoline) crystallized out thereupon, this being, according to the chemical properties and the analytical data, the 5,6-dimethyl-α-pyrone (IX, yield 27%).

Found %: C 67.69, 67.56; H 6.56, 6.64. $C_7H_8O_2$. Calculated %: C 67.76; H 6.49.

* It is possible to think that the resulting dialkyl-α-pyrones contain as impurities the products of cleavage of hydrogen bromide from dibromolactones which are isomeric to the dialkylpyrones
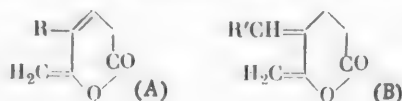
Since the first of these doubly unsaturated lactones (A) should not yield an adduct with maleic anhydride, while the formation of the adduct for the second substance (B) should not be accompanied by carbon dioxide evolution, it is possible to regard that the α-pyrones prepared by us either do not contain any doubly unsaturated lactones (A and B) or contain but a very insignificant amount of them, if at all.
** If the resulting dibromolactones are set aside for a week and are then subjected to heating and distillation, almost no corresponding α-pyrones are found in the distillate.
*** α-Pyrone (IX) may be isolated also by a slow distillation from the resulting distillate.

The filtrate, remaining after the filtration of the crystals of α-pyrone, was treated with a 5% aqueous sodium hydroxide solution in the cold; γ-acetylvaleric acid [7] (b.p. 140-142° at 5 mm, $n^{20}D$ 1.4495, m.p. of semicarbazone 135°) was isolated by acidification of the resulting alkaline solution; the formation of this substance in the alkaline hydrolysis indicated the formation of the unsaturated δ-lactone (I) (5,6-dimethyl-3,4-dihydro-α-pyrone) from the dibromolactone, along with that of α-pyrone (IX).

Preparation of 6-methyl-5-alkyl-α-pyrones. Dibromolactones (VI-VIII) were carefully heated under vacuum to 130-140° on an air bath in a stream of dry nitrogen for 4-6 hours. The reaction mixture was repeatedly vacuum distilled after completion of the heating (distillation was done in small portions to avoid tar formation during the distillation) until a complete cleavage of hydrogen bromide was attained. The resulting distillates were subjected to a fractional distillation through a column with glass packing (20 theoretical plates).

6-Methyl-5-ethyl-α-pyrone (X). The following fractions were obtained after the distillation of 12 g of the distillate formed from 73 g of dibromolactone, a column being used for the fractionation: 1st – 3.9 g, b.p. 95-100° at 4 mm, $n^{20}D$ 1.4792, 2nd – 1.5 g, b.p. 100-111.5° at 4 mm, $n^{20}D$ 1.4980, 3rd – 5.9 g, b.p. 111.5-113° at 4 mm, $n^{20}D$ 1.5180. The first fraction contained mainly the original unsaturated δ-lactone, judging by its constant and chemical properties; this (II) (6-methyl-5-ethyl-3,4-dihydro-α-pyrone; according to data from [3]: b.p. 94-96° at 8 mm, $n^{20}D$ 1.4667) formed a crystalline amide of γ-acetylcaproic acid with aqueous ammonium hydroxide solution, the amide having m.p. 105-106° (literature data [3]: m.p. 105-106°). The 3rd fraction was 6-methyl-5-ethyl-α-pyrone (X) (yield 25% accounting for the recovery of unreacted original δ-lactone), which had the following constants after a redistillation:

B.p. 121-123° at 7 mm, 130-131.5° at 12 mm, $n^{20}D$ 1.5182, d^{20}_4 1.0780, MR$_D$ 38.80. $C_8H_{10}O_2F_2$. Calculated: MR$_D$ 37.66; EM$_D$ 1.14.
Found %: C 69.10, 69.15; H 7.50, 7.35. $C_8H_{10}O_2$. Calculated %: C 69.56; H 7.24.

6-Methyl-5-propyl-α-pyrone (XI). The following fractions were obtained after a distillation through a column of 21 g of the distillate obtained from 57 g of dibromolactone VII: 1st – 3.5 g, b.p. 105-109° at 10 mm, $n^{20}D$ 1.4750, 2nd – 3 g, b.p. 116-130° at 10 mm, $n^{20}D$ 1.5000, 3rd – 6.5 g, b.p. 130-135° at 10 mm, $n^{20}D$ 1.5160. The first fraction contained mainly the unreacted initial unsaturated δ-lactone (III) (literature data [3]: b.p. 84-85° at 3 mm, $n^{20}D$ 1.4684) and formed the crystalline amide of γ-acetylenantic acid with m.p. 123-125° (according to data [3]: m.p. 124-125°) with aqueous ammonium hydroxide solution; the second fraction contained mainly α-pyrone (XI) with an insignificant impurity of the initial δ-lactone, judging by the index of refraction. The third fraction was 6-methyl-5-propyl-α-pyrone (XI) (yield 38%; calculated with accounting for recovered unreacted original δ-lactone) which after a redistillation through the column had the following constants:

B.p. 120-121° at 6 mm, $n^{20}D$ 1.5170, d^{20}_4 1.0515, MR$_D$ 43.80. $C_9H_{12}O_2F_2$. Calculated: MR$_D$ 42.28; EM$_D$ 1.52.
Found %: C 70.92, 70.91; H 8.15, 8.22. $C_9H_{12}O_2$. Calculated %: C 71.01; H 7.95.

6-Methyl-5-butyl-α-pyrone (XII). The following fractions were obtained after a distillation through a column of 28 g of the distillate obtained from 75 g of dibromolactone (VIII): 1st – 7 g, b.p. 105-113° at 4 mm, $n^{20}D$ 1.4726, 2nd – 5.5 g, b.p. 113-127° at 4 mm, $n^{20}D$ 1.4820, 3rd – 12.5 g, b.p. 127-131° at 4 mm, $n^{20}D$ 1.5120. The first and second fractions contained mainly the original unsaturated lactone (IV) (according to data [3]: b.p. 126-127° at 10 mm, $n^{20}D$ 1.4673); they dissolved in an aqueous ammonium hydroxide solution, forming the amide of γ-acetylcaprylic acid with m.p. 114-115° (according to data [3]: m.p. 114-115°). 6-Methyl-5-butyl-α-pyrone (XII) was isolated by distillation of the third fraction through a column (yield 46%, taking into account the recovered original unsaturated lactone); it had the following constants:

B.p. 119-121° at 3 mm, $n^{20}D$ 1.5128, d^{20}_4 1.0275, MR$_D$ 48.60. $C_{10}H_{14}O_2F_2$. Calculated: MR$_D$ 46.90; EM$_D$ 1.7.
Found %: C 71.97, 72.19; H 8.54, 8.55. $C_{10}H_{14}O_2$. Calculated %: C 72.29; H 8.43.

Preparation of double adducts of 5,6-dialkyl-α-pyrones with maleic anhydride (XIII-XVI). A solution of 0.006 mole of the appropriate α-pyrone and 0.012 mole of maleic anhydride in 3 ml of dry xylene was refluxed for 40-50 minutes; violent evolution of carbon dioxide was noted during this operation (125-135 ml; calculated 140 ml), this being completed after 15-20 minutes after the beginning of heating. The adduct

crystals which precipitated on cooling of the reaction mixture were recrystallized from acetone by addition of petroleum ether. The melting points, yields and analytical data of the resulting double adducts (XIII-XVI) are given in the table. The adducts dissolved readily on heating with 20% aqueous alkali solution; the tetrabasic acids precipitated on acidification of the solution with concentrated hydrochloric acid and these acids were transformed into the corresponding tetramethyl esters (XVII-XIX) by treatment with an ethereal solution of diazomethane; the esters crystallized readily from alcohol. The melting points and the analyses of the resulting tetramethyl esters are given in the table.

alkyl	no. of formula	m. p.	Double adducts of 6-methyl-5-alkyl-α-pyrones with maleic anhydride — found (in %)		calc. (in %)		yield (in %)	no. of formula	m. p.	Tetramethyl esters obtained from the double adducts — found (in %)		calc. (in %)	
			C	H	C	H				C	H	C	H
CH₃	(XIII)	290°	61.14, 60.90	4.49	60.87	4.37	83	(XVII)	205°	58.92, 58.71	6.74, 6.77	58.66	6.56
C₂H₅	(XIV)	276—277	62.55, 62.44	4.95, 4.97	62.10	4.86	80	--	--	--	--	--	--
C₃H₇	(XV)	231—232	63.09, 62.89	5.35, 5.30	63.16	5.26	85	(XVIII)	153—154	60.92, 60.69	7.25, 7.30	60.60	7.07
C₄H₉	(XVI)	208—209	63.80, 63.95	5.82, 5.90	64.15	5.66	82	(XIX)	118—119	62.07, 61.95	7.61, 7.41	61.51	7.31

SUMMARY

1. The method of preparation of 6-methyl-5-alkyl-α-pyrones by the cleavage of hydrogen bromide from the corresponding 5,6-dibromo-6-methyl-5-alkyl-δ-lactones was developed (by heating and distillation of the latter).

2. The previously undescribed α-pyrones: 5,6-dimethyl-, 6-methyl-5-ethyl-6-methyl-5-propyl- and 6-methyl-5-butyl-α-pyrones, were prepared in this way.

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CONCERNING THE STUDY OF OXIDATIVE NITRATION OF AROMATIC COMPOUNDS

II. NITRATION OF p-XYLENE IN THE PRESENCE OF MERCURIC NITRATE

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Nitro compounds and nitrophenols are formed during nitration of some aromatic compounds with aqueous nitric acid in the presence of mercuric nitrate (oxidative nitration); no data exist on the behavior of p-xylene under these conditions. Dilute nitric acid alone nitrates p-xylene in the side chain and oxidizes it predominantly to p-toluic acid at elevated temperature [1, 2].

We prepared p-toluic and terephthalic acids, p-tolualdehyde, p-methylbenzyl nitrate, p-tolyldinitro- and p-tolyltrinitromethanes, nitro- and 2,5-dinitro-p-xylenes, mercuric oxalate, diazonium slats and, evidently, a mercury salt of the addition product of mercuric nitrate and maleic acid, by the reaction of p-xylene with 51% nitric acid in the presence of mercuric nitrate at 28°. The qualitative composition of the reaction products is not changed by alteration of the proportion of nitric acid and p-xylene or of the duration of the experiment. Nitrophenols were not detected. p-Methylbenzyl nitrate was identified as diethyl-(4-methylbenzyl)-amine, obtained by a reaction with diethylamine [3]. The formation of p-tolyltrinitromethane was proved by the fact that p-toluic acid and p-tolyldinitromethane are isolated anew after treatment of the reaction mixture with potassium hydroxide, after a complete extraction of these substances from the mixture. The transition of p-tolyltrinitromethane into p-tolyldinitromethane under the influence of caustic alkali corresponds to the transformation of tetranitromethane into nitroform under similar conditions [4] and that of phenyltrinitromethane into phenyldinitromethane [5]; this was confirmed by our experiment with pure p-tolyltrinitromethane.

The supposition about the formation of a mercury salt of the addition product of mercuric nitrate and maleic acid was confirmed by the discovery of the nitrate ion and maleic acid after cleavage of the compound with hydrochloric acid, this being represented by the following equation:

$$\begin{array}{c} HO-CH-COO \\ | \\ O_3NHg-CH-COO \end{array} \Big\rangle Hg + 4HCl \rightarrow \begin{array}{c} CH-COOH \\ \| \\ CH-COOH \end{array} + 2HgCl_2 + HNO_3 + H_2O$$
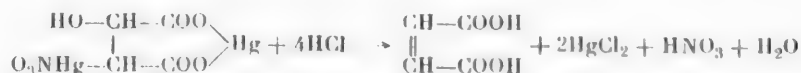
The ability of mercury salts to add to maleic acid is known [7].

Two azo dyes, different from the azo dye synthesized from 2,5-dimethylaniline and 2-naphthol, were prepared by coupling diazonium salts with 2-naphthol. The composition of the main reaction products was similar after nitration of p-xylene without the addition of mercuric nitrate; however, the degree of transformation of p-xylene was considerably smaller. The diazo compounds were not detected. The absence of nitrophenols in any notable quantity among the products of nitration of p-xylene in the presence of mercuric nitrate must be explained by the facile nitration of this substance in the side chain [1] and by the oxidizability of nitrophenols.

EXPERIMENTAL

The experiments were run in a thermostat at 28° in a flask with a reflux condenser; the latter was connected, through a take-off tube, to a system of Tishchenko absorption flasks filled with concentrated sulfuric

acid and 40% potassium hydroxide solution. Chemically pure p-xylene (m.p. 13.2°, $n^{21.4}$D 1.4930), nitric acid and mercuric nitrate were used as the starting materials. The nitrating mixture contained 51% of nitric acid and 5% of mercuric nitrate, calculated on mercury.

1. Nitration of p-xylene in the presence of mercuric nitrate. Experiment 1. A mixture of 80 g of p-xylene and 372 g of the nitrating mixture (proportion of nitric acid to p-xylene 4 : 1) was set aside for 285 hours. Then, the reaction mixture was cooled in ice and filtered. The precipitate was triturated, washed with 51% nitric acid and water and was dried. 0.03 g of terephthalic acid, identified by its properties and its ultra-violet absorption spectrum, was isolated by treament of the precipitate with ether. The absorption maxima of the aqueous solution of disodium salt of this terephthalic acid (10^{-4} mole/liter) were 280 and 237 mμ; according to the literature data [8]: 280 and 236.5 mμ.

8 g of p-toluic acid with m.p. 179-180° was extracted with alkali from the ethereal solution; the acid was identified by its mixed melting point with an authentic specimen. The organic layer, after addition of 50 ml of p-xylene and washing with 51% nitric acid and water, was treated twice with 10% sodium bicarbonate solution, then twice with 20% potassium bicarbonate solution with addition of 50% potassium carbonate solution, and finally with a mixture of 20% potassium hydroxide solution and diethylamine, in order to extract the products with acidic character [3]. 1.0 g of p-toluic acid with m.p. 178.5-179.5° and 4.7 g of p-tolyldinitromethane with m.p. 78-79° were isolated from the first and the second bicarbonate solutions; these were identified by their mixed melting points with authentic materials.

5.7 g of potassium salt of p-tolyldinitromethane was isolated from the first bicarbonate-carbonate solution. Plates (from alcohol).

Found %: N 12.01, 11.77. $C_8H_7O_4N_2K$. Calculated %: N 11.96.

p-Tolyldinitromethane with m.p. 74.5-77.7° was isolated by acidifying the solution of the potassium salt. Colorless plates (from petroleum ether), m.p. 79.5-80.1° (in literature [6]: 77°).

Found %: N 13.87, 13.97. $C_8H_8O_4N_2$. Calculated %: N 14.28.

p-Toluic acid with m.p. 179.5-180.6° [6] was obtained by heating p-tolyldinitromethane to 140-150°. p-Tolylbromodinitromethane was obtained by addition of an equivalent amount of bromine to the aqueous solution of the potassium salt of p-tolyldinitromethane at 0°. Yellowish oily liquid, n^{19}D 1.5650.

Found %: N 10.15, 9.83; Br 29.55, 29.56. $C_8H_7O_4N_2Br$. Calculated %: N 10.18; Br 29.05.

p-Tolylbromodinitromethane reverts to the potassium salt of p-tolyldinitromethane under the influence of an alcoholic solution of potassium hydroxide.

No organic compounds were extracted by a second and prolonged treatment of the organic layer with potassium bicarbonate solution in the presence of potassium carbonate. Treatment of the organic layer with 20% potassium hydroxide solution mixed with a small amount of diethylamine over three hours gave 1.82 g of the potassium salt of p-tolyldinitromethane, which was changed by acidification to p-tolyldinitromethane with m.p. 78-79°. 0.55 of p-toluic acid with m.p. 178-179.5° was isolated from the filtrate from the potassium salt.

The organic layer, after the above treatment, was heated for three hours on a water bath with 25 ml of diethylamine and was then washed with water and 10% hydrochloric acid in order to determine the p-methyl-benzyl nitrate content [3]. The nitrate ion was detected with diphenylamine and Nitron in the aqueous extract. Nitron nitrate (needles) obtained according to Busch [9], melting at 265.5-266° (in literature [9]: m.p. above 260°).

Found %: N 19.14, 19.01. $C_{20}H_{17}O_3N_5$. Calculated %: N 18.66.

1.8 g of diethyl-(4-methylbenzyl)-amine was obtained from the acid extract. A liquid with a yellowish tinge.

B.p. 79-80° (5 mm), d^{20}_4 0.8928, n^{20}D 1.4975, MR_D 58.16; calc. 57.96.
Found %: C 80.93, 80.88; H 10.82, 11.00; N 8.00, 8.14. $C_{12}H_{19}N$. Calculated %: C 81.29; H 10.80; N 7.90.

Picrate: yellow prismatic crystals (from alcohol), m.p. 100.3-101.1°.

Found %: C 52.92, 52.73; H 5.58, 5.66; N 13.90, 13.62. $C_{19}H_{22}O_7N_4$. Calculated %: C 53.13; H 5.46; N 13.78.

Triethyl-(4-methylbenzyl)-ammonium iodide: from diethyl-(4-methylbenzyl)-amine and ethyl iodide. Colorless crystals with m.p. 181.8-182.8° (with decomposition), soluble in water and insoluble in ether.

Found %: N 4.33, 4.29; I 37.88, 37.67. $C_{14}H_{22}NI$. Calculated %: N 4.20; I 38.08.

p-Tolualdehyde was extracted from the organic layer with sodium bisulfite after treatment with the diethylamine and the aldehyde was transformed into the semicarbazone. The weight of the latter was 3.1 g. Needles (from alcohol), m.p. 222° (with decomposition) (in the literature [10]: 219-220°).

Found %: N 28.83, 23.62. $C_9H_{11}ON_3$. Calculated %: N 23.71.

The organic layer, after having been treated with the bisulfite, was washed with water, dried with sodium sulfate and distilled twice under vacuum. 56 g of p-xylene was obtained along with 1.2 g of nitro-p-xylene* and 2.7 g of a fraction with b.p. 151° (25 mm).

2,5-Dinitro-p-xylene was steam distilled from the residue in the distilling flask, after which it was recrystallized from alcohol. Weight: 0.22 g, m.p. 149.5-150.1° (in the literature [11]: 147-148°).

Found %: N 14.05, 13.91. $C_8H_8O_4N_2$. Calculated %: N 14.28.

5.2 g of a mixture of mercury compounds, consisting mainly of mercuric oxalate, was precipitated by dilution of the aqueous acidic layer with water.

The yield of the products of oxidation of the side chain of p-xylene (p-toluic and terephthalic acids, p-tolualdehyde, p-methylbenzyl nitrate) in this experiment amounted to 59.8% of the total sum of the reaction products while p-tolyldinitro- and p-tolyltrinitromethanes constituted 32.9%, nitro- and 2,5-dinitro-p-xylene 4.9%, and the mixture of mercuric oxalate and the transformation product of maleic acid 2.4%.

Experiment 2. 4.3 g of p-toluic acid, 5.6 g of p-tolyldinitromethane, 1.6 g of p-tolualdehyde and 7.4 g of a mixture of mercury compounds were obtained after nitration of 40 g of p-xylene with 370 g of the nitrating mixture (ratio of nitric acid to p-xylene 8: 1) for 165 hours.

Experiment 3. 8.4 g of p-toluic acid, 7.1 g of p-tolyldinitromethane, 0.6 g of p-tolualdehyde, 0.44 g of p-methylbenzyl nitrate, 1.2 g of nitro-p-xylene, 0.1 g of 2,5-dinitro-p-xylene and 9.4 g of a mixture of mercury compounds were isolated after nitration of 40 g of p-xylene under the conditions given in Experiment 2 with the reaction duration of 285 hours.

Experiment 4. Diazonium salts were readily detected in the aqueous acid layer from Experiments 1,2 and 3 by their coupling with R-salt and with 2-naphthol. In order to isolate the coupling products of the diazonium salts with 2-naphthol we ran a special experiment under the conditions given in Experiment 3. A product which turned out to be a mixture of two orange dyes was obtained in the coupling. The mixture was treated, for the separation of the dye, first with a very dilute alkali solution, followed by glacial acetic acid. 1.1 g of a dye with m.p. 183° (decomposition), containing mercury and halogen, was then isolated by acidification of the alkaline solution with hydrochloric acid. 0.2 g of a dye was precipitated with water from the acetic acid extract, this product melting at 223.5° after a chromatographic purification in an alcohol solution over aluminum oxide. Both dyes were difficultly soluble in the usual organic solvents, insoluble in water; they are reduced by hydrosulfite. 1-p-Xylylazo-2-naphthol was synthesized for comparison from chemically pure 2,5-dimethylaniline and 2-naphthol. Red-violet needles (from alcohol), m.p. 154.2-154.7°.

Found % C 77.76, 77.83; H 5.90, 5.91; N 10.36, 10.51. $C_{18}H_{16}ON_2$. Calculated %: C 78.23; H 5.84; N 10.14.

The dye is soluble in the usual organic solvents and in concentrated sulfuric acid. The absorption maximum in ethyl alcohol solution was 497 mμ.

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*B.p. 239-240 at 749 mm. Found %: N 8.98, 9.17. $C_8H_9O_2N$. Calculated %: N 9.27.

Analysis of the mixture of mercury compounds. A sample of the mixture of mercury compounds from Experiments 1, 2 and 3 was triturated and washed with boiling water until free of the nitrate ion in the wash water, after which it was washed with alcohol and ether. The nitrate ion was readily found in the washed sample through the diphenylamine test. Mercury was precipitated with alkali after dissolution of the mixture in hydrochloric acid, the oxalate ion was precipitated with calcium chloride. Calcium oxalate was washed with water until free of calcium and chloride ions and was dried over sulfuric acid under vacuum [12].

Found %: Ca 26.54, 27.16. $CaC_2O_4 \cdot H_2O$. Calculated %: Ca 27.43.

After drying at $200°$: Found %: Ca 30.91, 31.25. CaC_2O_4. Calculated %: Ca 31.29.

The ultraviolet absorption spectra of the filtrate and of the aqueous solution of authentic maleic acid • were determined after the filtration of calcium oxalate. The following absorption maxima were found (mμ): fresh sample under examination in weakly acid medium 211, after ten days of standing of the same sample in acid medium 206.5 and in alkaline medium 204.5; solution of authentic maleic acid (0.5^{-4} mole / liter) 211. The absorption maxima according to the literature data [13]: maleic acid 210 mμ, its disodium salt 192, fumaric acid 207, its disodium salt 204. The transformation of maleic acid into fumaric under the influence of mineral acids and sodium chloride is long known [14].

Found %: C_2O_4 28.93; $C_4O_4H_2$ (according to spectral data) 0.68; N 0.63, 0.59. C_2O_4 Hg. Calculated %: C_2O_4 30.5 $C_4H_3O_6NHg_2$. Calculated %: N 2.36; $C_4O_4H_2$ 19.19.

The determination of nitrogen content in the mixture of mercury compounds gave the same results by the Dumas method and by the technique of nitrate analysis (reduction to ammonia).

2. Nitration of p-xylene in the absence of mercuric nitrate. A mixture of 40 g of p-xylene and 370 g of 51% nitric acid (ratio of nitric acid to p-xylene 8 : 1) was kept in a thermostat at $28°$ for 165 hours, after which it was subjected to the usual treatment. In this experiment we observed the evolution of a smaller amount of nitrogen oxides than in experiments run with addition of mercuric nitrate. Diazonium salts were not detected in the aqueous acid solution. 1.8 g of p-toluic acid, 0.85 g of p-tolualdehyde, 2.9 g of p-tolyldinitromethane, 0.41 g of p-methylbenzyl nitrate, 0.25 g of nitro-p-xylene, 0.05 g of 2,5-dinitro-p-xylene, 0.35 g of oxalic acid and 20.3 g of the original p-xylene were isolated. The amount of oxalic acid in the filtrate was determined by its isolation in the form of calcium oxalate and by titration of the latter with potassium permanganate.

p-Tolyltrinitromethane. This was prepared from p-tolyldinitromethane mainly like phenyltrinitromethane [5]. A mixture of 0.74 g of p-tolyldinitromethane, 7.5 ml of 67% nitric acid and 0.3 g of sodium nitrite (added periodically) was set aside at $20-22°$. The reaction mixture was diluted with water after ten days and extracted with carbon tetrachloride. The extract was treated with potassium carbonate solution, washed with water and dried over calcium chloride. 0.34 g of p-tolyldinitromethane with m.p. $78.5-79.5°$ was recovered from the carbonate solution. 0.21 g of p-tolyltrinitromethane – a yellow liquid with $n^{20}D$ 1.5347 – was obtained from the organic layer after the solvent had been distilled under vacuum at $20°$.

Found %: N 17.40, 16.55. $C_8H_7O_6N_3$. Calculated %: N 17.43.

Tolyltrinitromethane was transformed into the potassium salt of p-tolyldinitromethane in good yield by rapid treatment with an alcoholic solution of potassium hydroxide.

I express my gratitude to S. V. Bogdanov for advice and aid in the work.

SUMMARY

1. Mainly the products of oxidation and nitration of the side chain and of the destruction of the aromatic nucleus are formed in the nitration of p-xylene with nitric acid of moderate concentration both in the presence and the absence of mercuric nitrate at $28°$.

2. Diazonium salts are formed during nitration of p-xylene in the presence of mercuric nitrate.

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3. Diethyl-(4-methylbenzyl)-amine and its picrate, triethyl-(4-methylbenzyl)-ammonium iodide, 1-p-xylylazo-2-naphthol, p-tolylbromodinitromethane and p-tolyltrinitromethane were described.

4. The formation of p-methylbenzyl nitrate and of the transformation product of maleic acid was proven.

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N-ARYLSULFONAMIDO DERIVATIVES OF MONOETHANOLAMINE

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Among the N-alkylated dreivatives of arylsulfonamides which were examined with numerous examples [1-3, 8], the most interesting N,β-hydroxyalkyl substituted ones have not been studied sufficiently. There are indications in the literature that N,β-hydroxyethylarylsulfonamides and their derivatives of the type ArSO₂NRCH₂CH₂OOCR' have been proposed as plasticizers while the stearates of N,β-hydroxyalkylarylsulfonamides have been proposed as waxes [4]. Compounds containing the m-O₂NC₆H₄SO₂N= residue are being used as active coccicidal preparations [5]. It is also known that derivatives of p-chlorobenzenesulfonic acid are active insecticides and fungicides [2]. Hence, the synthesis of new N,β-hydroxyethylarylsulfonamides and their derivatives, and the study of their properties, possess not only the theoretical, but also the practical significance.

Knorr and Rossler [3] synthesized N,β-hydroxyethylbenzenesulfonamide by the Schotten-Baumann method. D. Peacock and U. Dutt [6] synthesized N,β-hydroxyethyl-p-toluenesulfonamide starting with ethylene chlorohydrin and p-toluenesulfonamide, and also prepared its chloro derivative. F. Allen and co-workers, followed later by McNalley, synthesized N,β-hydroxyethyl-3-nitro-4-chlorobenzenesulfonamide [7-8]. M. Kulka [2] synthesized N,β-hydroxyethyl-p-chlorobenzenesulfonamide and prepared its chloro derivative.

For the synthesis of N,β-hydroxyethylarylsulfonamides, we used the method developed by us for the preparation of N,N-bis-(β-hydroxethyl)-arylsulfonamides [9].

$$\text{ArSO}_2\text{Cl} + 2\text{NH}_2\text{CH}_2\text{CH}_2\text{OH} \longrightarrow \text{ArSO}_2\text{NHCH}_2\text{CH}_2\text{OH} + \text{HCl} \cdot \text{H}_2\text{NCH}_2\text{CH}_2\text{OH}$$

For this, we heated the appropriate arylsulfonyl chloride and monoethanolamine in a solution in benzene or o-xylene under a reflux condenser for five hours. The results of the experiments are given in Table 1.

TABLE 1

N,β-Hydroxyethylarylsulfonamides ArSO₂NHCH₂CH₂OH

No. of substance	Ar	Yield (in %)	M. p.	Content of nitrogen (in %)		Empirical formula
				found	calc.	
(I)	C₆H₅	47.5	Sirup	6.91	6.96	C₈H₁₁O₃NS
(II)	p-CH₃C₆H₄	63.4	Sirup	6.61	6.51	C₉H₁₃O₃NS
(III)	o-CH₃C₆H₄	85.8	76—78°	6.71	6.51	C₉H₁₃O₃NS
(IV)	p-ClC₆H₄	65.0	106—108	6.17	5.94	C₈H₁₀O₃NSCl
(V)	3,4-NO₂ClC₆H₃	63.6	124—125	10.25	9.98	C₈H₉O₅N₂SCl
(VI)	iso -C₃H₇C₆H₄	89.4	Sirup	5.57	5.76	C₁₁H₁₇O₃NS
(VII)	(CH₃)₃C₆H₂	60.0	79—79.5	6.20	5.76	C₁₁H₁₇O₃NS
(VIII)	m-NO₂C₆H₄	78.0	82—84	11.58	11.37	C₈H₁₀O₅N₂S
(IX)	Cl₃C₆H₂	74.0	132—133	4.72	4.59	C₈H₈O₃NSCl₃

Some of the preparations, obtained in the form of a sirup, solidified after prolonged standing and were recrystallized from water or benzene. Part of the compounds obtained in the form of a sirup failed to crystallize even after prolonged standing. N,β-Hydroxyethylarylsulfonamides were either transparent sirups or crystalline substances. They were all readily soluble in alkali, alcohol, more difficultly in benzene; they were poorly soluble in water, except for N,β-hydroxyethyl-m-nitrobenzenesulfonamide (soluble after mild heating), and insoluble in petroleum ether and carbon tetrachloride.

In order to study the chemical properties of N,β-hydroxyethylarylsulfonamides we prepared the sodium salts, chlorides and N-butyl or N-benzyl substituted derivatives. The sodium salts were obtained by the action of alcoholic alkali on the appropriate N,β-hydroxyethylarylsulfonamide in the cold. The replacement of the hydroxy group by chlorine was performed by the action of thionyl chloride. The replacement of the hydrogen of the amide group by butyl or benzyl radicals was performed by a prolonged heating of the sodium salt of N,β-hydroxyethylarylsulfonamide with excess butyl bromide or benzyl chloride. The resulting derivatives of N,β-hydroxyethylarylsulfonamides are given in Tables 2 and 3.

TABLE 2

N,β-Chloroethylarylsulfonamides $ArSO_2NHCH_2CH_2Cl$

No. of substance	Ar	M. p.	Nitrogen content (in %)		Empirical formula
			found	calc.	
(X)	C_6H_5	64—66°	6.45	6.37	$C_8H_{10}O_2NSCl$
(XI)	$p-CH_3C_6H_4$	96—98	6.29	5.99	$C_9H_{12}O_2N$
(XII)	$o-CH_3C_6H_4$	Sirup	5.96	5.99	$C_9H_{12}O_2NCl$
(XIII)	$p-ClC_6H_4$	151—152	5.56	5.51	$C_8H_9O_2NSCl_2$
(XIV)	$3,4-NO_2ClC_6H_3$	97—98	9.53	9.36	$C_8H_8O_4N_2SCl_2$
(XV)	$iso-C_3H_7C_6H_4$	57—58	5.70	5.32	$C_{11}H_{16}O_2NSCl$
(XVI)	$(CH_3)_3C_6H_2$	103—104	5.50	5.32	$C_{11}H_{16}O_2NSCl$
(XVII)	$m-NO_2C_6H_4$	74—75	10.61	10.58	$C_8H_9O_4N_2SCl$
(XVIII)	$Cl_3C_6H_2$	140	4.57	4.64	$C_8H_7O_2NSCl_4$

TABLE 3

N-Butyl and N-Benzyl-N,β-hydroxyethylarylsulfonamides $ArSO_2NRCH_2CH_2OH$

No. of substance	Ar	R	Nitrogen content (in %)		Empirical formula
			found	calc.	
(XIX)	C_6H_5		5.56	5.45	$C_{12}H_{19}O_2NS$
(XX)	$p-CH_3C_6H_4$		5.22	5.16	$C_{13}H_{21}O_3NS$
(XXI)	$o-CH_3C_6H_4$	C_4H_9	5.21	5.16	$C_{13}H_{21}O_3NS$
(XXII)	$p-ClC_6H_4$		4.97	4.80	$C_{12}H_{18}O_3NSCl$
(XXIII)	$3,4-NO_2ClC_6H_3$		8.20	8.32	$C_{12}H_{17}O_5N_2SCl$
(XXIV)	$iso-C_3H_7C_6H_4$		4.86	4.64	$C_{15}H_{25}O_3NS$
(XXV)	$m-NO_2C_6H_4$	C_4H_9	9.4	9.20	$C_{12}H_{18}O_5N_2S$
(XXVI)	$Cl_3C_6H_2$		4.10	3.88	$C_{12}H_{16}O_3NSCl_3$
(XXVII)	$(CH_3)_3C_6H_2$		5.16	4.68	$C_{15}H_{25}O_3NS$
(XXVIII)	$iso-C_3H_7C_6H_4$	$CH_2C_6H_5$	4.02	4.20	$C_{18}H_{23}O_3NS$
(XXIX)	C_6H_5		4.80	4.81	$C_{15}H_{17}O_3NS$

All the N,β-hydroxyethylarylsulfonamides were crystalline substances. Their purification was done by recrystallization from an appropriate solvent. They were all readily soluble in benzene, acetone and alcohol, less readily in carbon tetrachloride and petroleum ether, and insoluble in water.

All the N-butyl- and N-benzyl-N,β-hydroxyethylarylsulfonamides were transparent sirupy liquids.

EXPERIMENTAL

Reaction of monoethanolamine with arylsulfonyl chlorides. 0.05 mole of arylsulfonyl chloride, 0.11 mole of monoethanolamine and 25-30 ml of o-xylene or benzene were refluxed for five hours in a flask with a reflux condenser with constant stirring. A precipitate formed on cooling in the case of (IV) and (IX), the precipitate being separated by filtration; in other cases a layer of a viscous liquid formed on the bottom of the flask, this being separated with a separatory funnel. The o-xylene solution was treated with a 10% solution of caustic alkali, washed with water, dried and vacuum distilled. The viscous liquid or the precipitate (IV) and (IX) was dissolved in 10% alkali and the product was isolated from the resulting solution by acidification to Congo red with concentrated hydrochloric acid. The product precipitated as a thick sirup, or as a crystalline precipitate in the case of (IV) and (V); this was separated, washed, dried and recrystallized. The sirupy product was separated in a separatory funnel, washed, dissolved in acetone, dried in solution over calcined potassium carbonate and freed of acetone by vacuum distillation. In the case of (VIII) and (IX), treating the lower layer with 10% solution of alkali yielded the sodium salt of N,β-hydroxyethylarylsulfonamide. The resulting salt was dissolved in water, filtered from an insignificant insoluble portion and the filtrate was acidified to acid test with Congo red by means of concentrated hydrochloric acid; the resulting precipitate of N,β-hydroxyethylarylsulfonamide was filtered off, washed, dried and recrystallized. For an exact account of the reaction products remaining after the isolation of N,β-hydroxyethylarylsulfonamide, we evaporated the acidified solution under vacuum and dissolved the residue in a mixture of alcohol-acetone; the sodium chloride was separated and the solvents were removed under vacuum. The residue was a viscous liquid which contained an excess of ethanolamine and byproducts of the reaction, which were not examined. N,β-hydroxyethylarylsulfonamides (I)-(IX) (Table 1) were synthesized by this method.

Preparation of sodium salts of N,β-hydroxyethylarylsulfonamides. A sample of the appropriate N,β-hydroxyethylarylsulfonamide was treated with alcoholic alkali in the cold; a precipitate formed on standing and this was filtered and dried. Sodium salts of all N,β-hydroxyethylarylsulfonamides were crystalline substances, which were readily soluble in water. The general formula of these salts was $ArSO_2NNaCH_2CH_2OH$. Some of the salts contained water of crystallization. The sodium salt of N,β-hydroxyethyl-p-toluenesulfonamide had m.p. about 230° (with decomposition).

Found %: N 5.84. $C_9H_{12}O_3NSNa$. Calculated %: N 5.90.

Preparation of N,β-chloroethylarylsulfonamides. 0.003 mole of the appropriate N,β-hydroxyethylarylsulfonamide was placed in a reaction flask provided with a stirrer, a dropping funnel and a reflux condenser connected to an absorption flask. 0.009 mole of thionyl chloride was added dropwise in the cold, after which the whole was heated for 1.5 hours on a hot water bath. After cooling, 15-20 ml of water was added for complete decomposition of excess thionyl chloride, whereupon the reaction mixture solidified. The precipitate was filtered off, washed thoroughly with water, dried and recrystallized from petroleum ether or aqueous methanol. The yields of pure N-β-chloroethylarylsulfonamides were about 40%. Chlorides of N,β-hydroxyethylarylsulfonamides (X)-(XVIII) (Table 2) were prepared by this method.

Preparation of N-substituted N,β-hydroxyethylarylsulfonamides. 0.002 mole of sodium salt of the appropriate N,β-hydroxyethylarylsulfonamide was placed in a round-bottomed flask, treated with 5 ml of butyl bromide and refluxed for 12 hours. The solid precipitate was filtered off after cooling, while butyl bromide was distilled from the filtrate under vacuum. The products were obtained in the form of colored transparent sirups; yield: 42%. Thus were prepared the N-butyl-N,β-hydroxyethylarylsulfonamides (XIX)-(XXVII) (Table 3).

For the preparation of N-benzyl-N,β-hydroxyethylarylsulfonamides, 0.002 mole of sodium salt of the appropriate N,β-hydroxyethylarylsulfonamide was heated with excess benzyl chloride (6 ml) at 120-140° for six hours. Transparent sirups of (XXVIII)-(XXIX) (Table 3) were obtained after the separation of the precipitate and distillation of excess benzyl chloride under vacuum.

SUMMARY

The reaction of monoethanolamine with arylsulfonyl chlorides was examined. 23 previously undescribed derivatives of arylsulfonamides were prepared and characterized.

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*Original Russian pagination. See C.B. Translation.

A STUDY IN THE FIELD OF THE DIECKMAN REACTION

VI. CYCLIZATION OF DIETHYL ESTERS OF α-ACETYL- AND α-BENZOYLPIMELIC ACIDS.

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During the development of our work on the examination of the mechanism of the Dieckmann reaction [1] we studied the cyclization of α-acetyl- (I) and α-benzoylpimelates (II). We have shown earlier [1] that cyclization of α-carbethoxypimelate (diethyl) proceeds, contrary to expectations, at the unsubstituted α-carbon atom and leads to 2,6-dicarbethoxycyclohexanone. Thus it was interesting to determine whether or not it is possible to run the cyclization of (I) at the substituted α-carbon atom with formation of either 2-carbethoxy-cyclohexanone (III) (with cleavage of ethyl acetate) or 2-acetylcyclohexanone (IV) (with cleavage of diethyl carbonate).
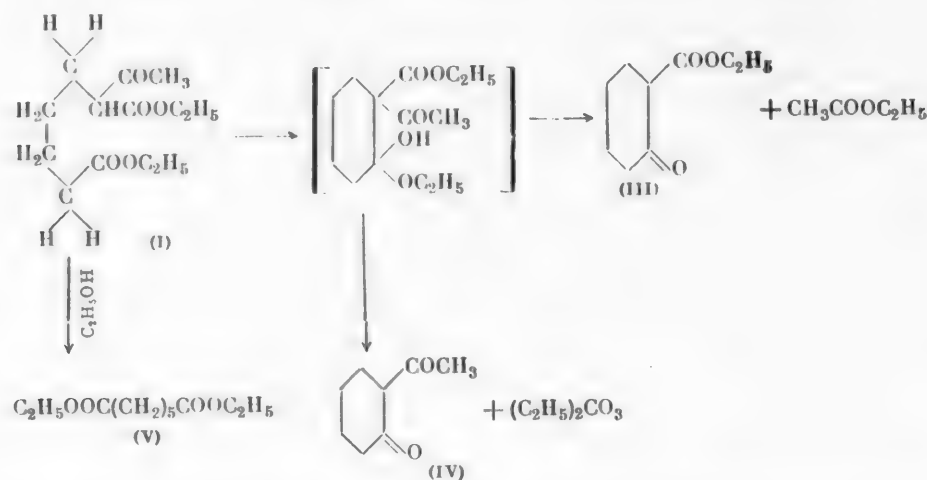
Actually, (III) is formed in 52-57% yield and ethyl acetate is evolved during the cyclization of (I) in boiling xylene in the presence of 1.4 gram atoms of powdered sodium or 1.4 moles of sodium ethoxide. Only in running the reaction in an alcoholic solution of 1.5 moles of sodium ethoxide was it possible to make diethyl pimelate (V) the main reaction product (yield 35%), while the yield of (III), isolated as 2-phenyl-4,5,6, 7-tetrahydro-3-indazolone, was extremely low (6.5%).

Formation of (V) could be the result of alcoholysis of either (I) or the preliminarily formed (III). It was shown that (III) is practically not cleaved under these conditions (only small amounts of V are formed) (yield 3.1%), while (I) forms (V) in 22% yield on being boiled with an alcoholic solution of 0.2 mole of sodium ethoxide, while in the presence of 1 mole of sodium ethoxide the yield is 56%. Formation of small amounts of (III) in the treatment of (I) with an alcoholic solution of 1.5 moles of sodium ethoxide is explained by cyclization of (V) which proceeds under such conditions with but a very low yield (6%), as established by us.

The problem of the mechanism of the reaction in the presence of powdered sodium was solved by running the process with a deficiency (0.9 gram atom) of sodium. Under such conditions, the main reaction products were ethyl acetate (27.3%), (V) (13.9%), and (III) (16%). Thus, even in a nonalcoholic medium the

first step of the process is evidently the reaction of alcoholysis of (I) with formation of (V) which then cyclizes to (III), which is confirmed by the preparation of this directly from (V) under similar conditions.

The fact that the alcoholysis of (I) may proceed only in the presence of alcohol made it necessary to suppose that in running the reaction in boiling xylene in the presence of powdered sodium traces of 2-acetyl-6-carboethoxycyclohexanone are formed first (i.e., that the reaction proceeds in the direction similar to that studied previously [1]), while alcohol is evolved. The latter causes alcoholysis of (I) and the (V) resulting from this cyclizes with evolution of alcohol which again enters into reaction with (I). The ease of alcoholysis of (I) under these conditions is well confirmed by formation of (V) in 50% yield during the gradual addition of 1 mole of alcohol to a boiling mixture of one mole of (I) and 0.2 gram atoms of powdered sodium in xylene.

The reaction of (II) with excess powdered sodium proceeds similarly to that of (I) and leads to a mixture of (III) with ethyl benzoate. These results permit us to propose the following mechanism of cyclization of α-acetyl- and α-benzoylpimelates (diethyl esters).

$$
(I) \Biggl\{
$$

$$
\left[
\begin{array}{c}
H_2C{-}C(H)(H){-}\overline{C}HCOOC_2H_5 \\
H_2C{-}C(H){-}COOC_2H_5 \\
\quad\quad COCH_3
\end{array}
\right]
\longrightarrow
\begin{array}{c}
COOC_2H_5 \\
OC_2H_5 \\
O^- \\
COCH_3
\end{array}
\longrightarrow
\begin{array}{c}
COOC_2H_5 \\
O \\
COCH_3
\end{array}
+ C_2H_5OH
$$

$$
\begin{array}{c}
H_2C{-}C(H)(H){-}CH_2COOC_2H_5 \\
H_2C{-}\overline{C}{-}COOC_2H_5 \\
\quad\quad COCH_3
\end{array}
\xrightarrow[{-CH_3COOC_2H_5}]{+C_2H_5OH}
\begin{array}{c}
H_2C{-}C(H)(H){-}CH_2COOC_2H_5 \\
H_2C{-}\overline{C}{-}COOC_2H_5 \\
\quad\quad H
\end{array}
\xrightarrow{-C_2H_5OH}
$$

$$
\longrightarrow
\begin{array}{c}
COOC_2H_5 \\
O
\end{array}
\longrightarrow (III)
$$
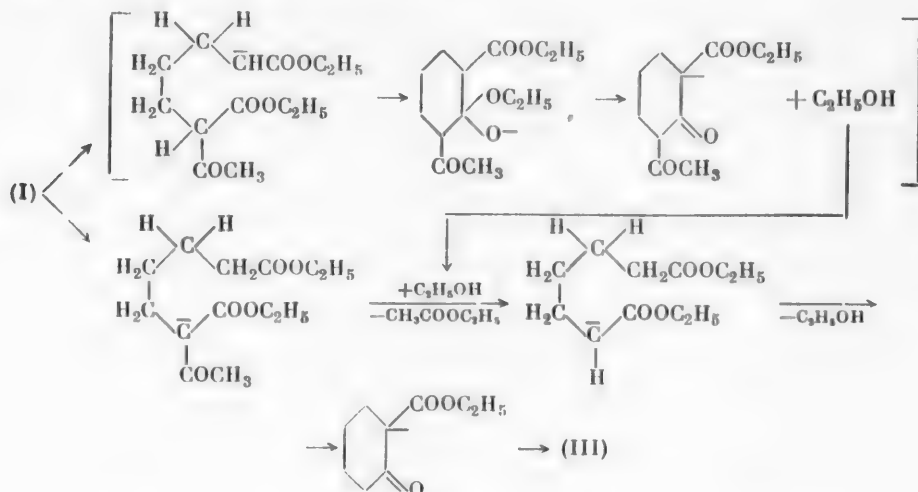
The structure of (III) was confirmed by the preparation of 2-phenyl-4,5,6,7-tetrahydro-3-indazolone [2] from it, the latter being identified in turn by a convergent synthesis from cyclohexanone.

The original (I) and (II) were prepared by us in 76.7% and 81.5% yields, respectively, by condensation of ethyl δ-chlorovalerate with sodioacetoacetic and sodiobenzoylacetic esters in the presence of sodium iodide. (I) is formed in 60% yield by using ethyl δ-bromovalerate under the same conditions. The method of preparation of (I), described in the literature and starting with ethyl δ-bromovalerate (without sodium iodide) gives a yield of 25% [3].

EXPERIMENTAL

Preparation of diethyl α-acetylpimelate (I). a) From ethyl δ-chlorovalerate. 41.2 g of ethyl δ-chlorovalerate [1] and 19.7 g of sodium iodide were added at 10-15° to a solution of sodioacetoacetic ester (from 65 g of acetoacetic ester, 5.75 g of sodium and 100 ml of anhydrous alcohol) and the whole was refluxed with stirring for 20 hours. The alcohol was distilled off (toward the end under slight vacuum) and the residue was poured into 200 ml of water, acidified with 40% sulfuric acid until weakly acid to Congo red and extracted twice with benzene (200 + 100 ml). The benzene solution was washed in succession with 30 ml of 5% sodium carbonate solution and with water until neutral to a brilliant yellow paper, after which it was dried and distilled. (I) was isolated in 47.9-49.6 g yield (74.4-76.6%), b.p. 141-146° at 2.5 mm, n_D^{20} 1.4445, d_4^{20} 1.0430. According to [3]: b.p. 175-179° at 12 mm.

b) From ethyl δ-bromovalerate. (I) was prepared analogously to the above from 61 g of ethyl δ-bromovalerate [1], 76 g of acetoacetic ester, 6.75 g of sodium, 117 ml of anhydrous alcohol and 25.2 g of sodium iodide; yield: 45.2 g (60%); b.p. 142-145° at 2.5 mm.

Preparation of diethyl α-benzoylpimelate (II). 41.2 g of ethyl δ-chlorovalerate and 19.7 g of sodium iodide was added at 10-15° to the solution of sodiobenzoylacetic ester, prepared from 96 g of benzoylacetic ester, similarly to that described for (I), and the whole was refluxed with stirring for 14.5 hours, treated with 8 g more of sodium iodide and refluxed for 13 hours longer. The mixture was treated similarly to the above and yielded (II) in 65.2 g yield (81.5%).

B.p. 193-194.5° at 1.5 mm, $n^{20}D$ 1.5000, d^{20}_4 1.0900, MR_D 86.34; calculated for enol 86.09, for ketone 85.04.

Found %: C 67.65; H 7.44. $C_{18}H_{24}O_5$. Calculated %: C 67.48; H 7.55.

Cyclization of diethyl α-acetylpimelate (I). 1) In xylene medium. a) With excess sodium. 38.7 g of (I) was added rapidly to a suspension of 4.7 g of powdered sodium in 150 ml of dry xylene. The mixture was stirred energetically until the exothermic reaction had ceased (10 minutes; temperature rose to 77°), after which the whole was heated to boiling on an oil bath (127-129.5°); the refluxing with stirring was continued until the boiling point of the reaction mixture ceased to drop (5-6 hours; boiling point drops to 117°). The evolved ethyl acetate was distilled through a column, collecting the fraction with b.p. 73-77° (4.9 g), $n^{20}D$ 1.3760. The residue was cooled and the thickened mass was poured into 150 g of ice, cooling on the outside with a salt-ice mixture (the reaction mixture temperature was −7° to −5°), after which it was neutralized with dilute hydrochloric acid (1 : 1) until acid to Congo red at −1° to −3°. The organic layer was separated and the aqueous layer was extracted with 75 ml of xylene (or benzene); the combined organic layer was washed successively with 30 ml of 5% sodium carbonate solution and with water until neutral to the brilliant yellow paper, after which it was dried over anhydrous sodium sulfate. The solvent was distilled off and the residue was vacuum distilled, yielding (III); yield: 52.2-52.5%; b.p. 62-67° at 1 mm, 72-77° at 2.5 mm. After redistillation: b.p. 71.5-75° at 2.5 mm, $n^{20}D$ 1.4780, d^{20}_4 1.0675. It gave a violet color with an aqueous solution of ferric chloride. According to literature data [4]: b.p. 104-106° at 9 mm, $n^{17.5}D$ 1.4750, $d^{17.5}_4$ 1.0741.

Similar results were obtained in the cyclization with addition of 2-3 drops of anhydrous alcohol, as well as in the presence of sodium ethoxide which was free of alcohol (in this case the boiling point is 110° in the beginning of the experiment and drops to 100° in two hours and the mass thickens at once; 100 ml of dry xylene was added and the boiling was continued (106.5°); the yield of (III) in this case was 55.7%; b.p. 71-76° at 2.5 mm, $n^{20}D$ 1.4780, d^{20}_4 1.0669.

2-Phenyl-4,5,6-7-tetrahydro-3-indazolone. 1.7 g of (III), prepared by cyclization of (I), was heated for one hour on a steam bath with 1.1 g of phenylhydrazine. The mixture was cooled to 20°, treated with 4 ml of ether, filtered and the resulting precipitate was washed with ether until a colorless filtrate appeared. Yield: 1.95 g (90.7%); m.p. 179-80°. M.p. after recrystallization from a mixture of ten volumes of benzene and 2.5 volumes of alcohol: 179-80°.

Found %: C 72.60; H 6.76. $C_{13}H_{14}ON_2$. Calculated %: C 72.87; H 6.59.

It did not give a mixed melting point depression with a sample of the indazolone prepared from (III) that had been synthesized by the known route from cyclohexanone [5]. According to the literature data [2]: m. p. 180°.

b) With deficiency of sodium. The cyclization of 25.8 g of (I) was run similarly to the above in the presence of 2.1 g of powdered sodium; the resulting ethyl acetate (2.4 g) was distilled off and (III) was isolated in 2.7 g yield (16%) (b.p. 67-73.5° at 1.5 mm, $n^{20}D$ 1.4800, d^{20}_4 1.0640; the indazolone, m.p. 177.5-179°), along with (V) in 3 g yield (13.9%); b.p. 100-101° at 2 mm, $n^{20}D$ 1.4340, d^{20}_4 0.9992 (according to the literature data [6]: b.p. 139-141° at 15 mm, $n^{20}D$ 1.43052, d^{20}_4 0.99448); the dihydrazide of pimelic acid, with m.p. 184.5-185° (from 70% alcohol) formed on treatment of this with hydrazine hydrate; the product did not give a mixed melting point depression with the authentic sample; according to the literature data [7]; m.p. 185°.

2. In alcohol medium. 33.5 g of (I) was added to the solution of sodium ethoxide (from 4.5 g of sodium and 100 ml of anhydrous alcohol) and the whole was refluxed on a water bath with stirring for three hours. Part of the alcohol was distilled off and the remainder was poured onto 100 g of ice, cooling externally with salt-ice. 100 ml of ether was added and the mixture was acidified with dilute sulfuric acid until acid to Congo red; the organic layer was separated and distilled, after the usual treatment, the following fractions being

collected: 1st – b.p. 72-87° at 2.5 mm, 2.1 g, n^{20}D 1.4600, 2nd – b.p. 87-103° at 2.5 mm, 5.5 g, 3rd – b.p. 103.5-108.5° at 2.5 mm 7.5 g. The second fraction was distilled again and yielded the following fractions: 4th – b.p. 75-83° at 2.5 mm, 0.8 g, n^{20}D 1.4595, 5th – b.p. 83-103.5° at 2.5 mm, 1.9 g, 6th – b.p. 103.5-109° at 2.5 mm, 2.2 g.

The first and fourth fractions gave an intense color reaction with aqueous ferric chloride solution; the fifth fraction gave a very weak test, while the third and sixth fractions failed to give the color test. The third and the sixth fractions (9.7 g, 34.7%) represented (V); they were combined (n^{20}D 1.4325, d^{20}_4 0.9984) and yielded the above-described hydrazide with m.p. 184-185° (from 70% alcohol).

The mixture of the first and the fourth fractions represented crude (III) which treated with phenylhydrazine gave 2-phenyl-4,5,5,7-tetrahydro-2-indazolone with m.p. 179-180°, in 53.5% yield.

Cyclization of diethyl α-benzoylpimelate (II). The cyclization of 48 g of (II) was run analogously to that of (I) in 155 ml of dry xylene with 4.7 g of powdered sodium and 2-3 drops of alcohol; the boiling point of the reaction mixture dropped from 129.5° to 118.5° after 5.5 hours. Fraction A with b.p. 87-90° at 10 mm (9.1 g, n^{20}D 1.4880, d^{20}_4 1.0614) was collected during the distillation, along with fraction B with b.p. 64-67.5° at 2 mm (5.7 g, n^{20}D 1.4895, d^{20}_4 1.0571) obtained after repeated distillation of the fore-runs and the higher-boiling fraction. Fractions A and B (14.8 g), which gave a violet color with aqueous ferric chloride solution and which represented a mixture of (III) with ethyl benzoate, were combined; treatment with phenylhydrazine gave the indazolone in 55.5% yield; m.p. 179.5-180°.

11.6 g of the mixture of A and B was extracted with 150 ml of 6% potassium hydroxide solution, the resulting emulsion was extracted with ether (twice with 25 ml), the ethereal solution was washed with 6% potassium hydroxide solution to a negative test with aqueous ferric chloride solution and the organic layer then yielded 2.9 g of ethyl benzoate with b.p. 49.5-50° at 1.5 mm, n^{20}D 1.5025, d^{20}_4 1.0431.

From literature data: b.p. 94.3°, at 13 mm, $n^{17.3}$D 1.50682 [8], d^{25}_4 1.0422 [9].

Alcoholysis of 2-carbethoxycyclohexanone (III). 22.1 g of (III), prepared from cyclohexanone [5], was refluxed for three hours under conditions which were similar to those used for cyclization of (I) in alcoholic medium. This was worked up similarly to the above and 12.9 g of unreacted (III) was isolated by distillation (b.p. 72-75° at 2.5 mm, n^{20}D 1.4760, d^{20}_4 1.0678; indazolone, m.p. 177.5-178.5°) along with (V) (yield: 0.9 g (3.1%)); b.p. 95-97.5° at 1.5 mm, n^{20}D 1.4330.

Alcoholysis of diethyl α-acetylpimelate (I). a) In alcoholic medium. 7.4 g of (I) was refluxed for three hours in a solution of sodium ethoxide (from 0.13 g of sodium and 43 ml of anhydrous alcohol) and worked up as described above, yielding (V); yield: 1.33 g (22%); b.p. 100-107° at 2 mm, n^{20}D 1.4325, d^{20}_4 0.9961; the dihydrazide, m.p. 185-185.5° (from 70% alcohol). Yield of (V) rises to 56% on increase of the amount of sodium to 1 gram·atom per one mole of (I).

b) In xylene. A mixture of 2.62 g of anhydrous alcohol and 15 ml of dry xylene was added dropwise over two hours to a mixture of 14.8 g of (I), 0.27 g of powdered sodium and 60 ml of dry xylene heated to boiling (138.5°). The whole was refluxed with stirring for 3 hours and 20 minutes longer, cooled, worked up as described above, and distilled. (V) was obtained in 6.03 g (49%) yield; b.p. 97.5-102.5° at 1.5 mm, n^{20}D 1.4325, d^{20}_4 0.9965; the dihydrazide, m.p. 184.5-185° (from 70% alcohol).

Diethyl pimelate. (V). 56.2 g of diethyl α-carbethoxypimelate was hydrolyzed according to [10], and the resulting pimelic acid was dehydrated by distillation of benzene without isolating the acid; the residue was esterified according to [11], yielding (V) in 32.3 g (76.7%, calculated on the starting material taken) yield; b.p. 104-106° at 3 mm, n^{20}D 1.4295, d^{20}_4 0.9928; the dihydrazide, m.p. 185-185.5° (from 70% alcohol).

Cyclization of diethyl pimelate (V). a) In alcoholic medium. 21.6 g of (V) was cyclized similarly to (I) described above (3.5 g of sodium, 77 ml of anhydrous alcohol, three hour boiling), worked up as described above and yielded (III) after the distillation; yield: 0.98 g (5.8%) ; b.p. 79.5-85° at 3 mm, n^{20}D 1.4705; the indazolone, m.p. 178.5-180°; 12.6 g of unreacted (V) was recovered.

b) In xylene. 21.6 g of (V) was cyclized in 100 ml of dry xylene in the presence of sodium ethoxide free of alcohol (from 6.25 g of alcohol and 3.13 g of powdered sodium) similarly to the reaction of (I) above. the reaction mass thickened after ten minutes of heating. 75 ml of dry xylene was added and the refluxing

was continued. The mixture was worked up similarly to the one described above, yielding (III): 9.8 g (57.6%) b.p. 66-71° at 1.5 mm, n_D^{20} 1.4800, d_4^{20} 1.0786; the indazolone, m.p. 179-180°.

SUMMARY

1. The cyclization of diethyl α-acetyl- and α-benzoylpimelates under the conditions of the Dieckmann reaction was studied. It was shown by the example of diethyl α-acetylpimelate that the primary reaction product is diethyl pimelate which forms as the result of alcoholysis of the original ester. 2-Carbethoxycyclohexanone is formed as the result of a subsequent cyclization of diethyl pimelate . The reaction mechanism was suggested.

2. The structure of 2-carbethoxycyclohexanone was confirmed by the convergent synthesis from cyclohexanone and by the preparation of the known 2-phenyl-4,5,6,7-tetrahydro-3-indazolone from it.

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A STUDY OF THE DEHYDROGENATION REACTION OF CYCLOHEXANE

(CONCERNING THE TECHNIQUE OF THE STUDY)

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In the course of reactions which are accompanied by evolution or absorption of heat, the temperature in the reaction zone varies along the cross section of the reactor and along the length of the catalyst layer. The magnitudes of the radial temperature drops, which depend on the thickness of the catalyst layer, the hydrodynamic conditions and the conditions of heat transfer, are small in comparison with the temperature differences which originate along the longitudinal section of the reactor and produce no decisive influences on the course and the direction of the chemical reaction. However, the temperature change along the longitudinal section of the reactor, i.e., along the path of flow of the reacting gas stream, reaches several tens of degrees at times. Thus in paper [1] dealing with the study of the kinetics of ammonia synthesis in a laboratory reactor with 13 mm diameter, a temperature peak above 100° was observed in the catalyst zone (this having the total length of but 40 mm): the temperature in the reaction zone reached 600°, while the temperature at the entry site to the catalyst zone was kept constant at 500°, and the exit temperature was kept at about 520°. Such examples are not unique [2].

We noted a sharp temperature drop in the catalyst layer in the very first preliminary experiments. A repeated and careful measurement of the temperature along the length of the catalyst layer was performed under the established regime of cyclohexane feed and hydrogen feed. The measurement was done with a thermocouple which was moved inside the well of the reactor. The temperature of the aluminum block, which heated the reactor, was kept constant. It turned out that the difference in temperatures along the length of the catalyst layer reached 30°, while the temperature difference between the minimum temperature in the catalyst layer (the point corresponding approximately to the middle of the catalyst layer of 2/3 of its length from the bottom) and the temperature in the heated block was 50-60°. It was quite evident that the reaction proceeded at a temperature which did not correspond to the apparent constant temperature of the reaction, fixed at one point (in the middle of the layer or at its ends). Therefore, in such cases in which the temperature was judged by the readings of a thermocouple placed at the entry or the exit of the reaction zone, the true mean reaction temperature was below the recorded one, while in cases in which the temperature was judged by the readings of the thermocouple set at in the middle of the catalyst layer the true mean reaction temperature was above the indicated one. The last circumstance evidently occurred in the work of number of authors during the study of the kinetics of the dehydrogenation reaction of cyclohexane over fresh and deactivated platinum catalysts [3]. The degree of conversion of cyclohexane cited by the authors for the experimental temperature read from fresh catalysts greatly exceeded the equilibrium concentrations of benzene at atmospheric pressure, as calculated by Frost [4] and Vvedenskii [5]. This places under suspicion the conclusions drawn from the work [3].

Our first observations and the analysis of the technique of temperature measurements done by other authors, who studied exothermic and endothermic reactions, pointed up the need for a special study of the problems of temperature distribution inside the reactor and of the ways of creating isothermal conditions for

the process without which it is impossible to run any further investigations. The study made by us showed that the temperature distribution in the catalyst zone during the dehydrogenation reaction of cyclohexane has complex nature. Under equal temperatures of the entry of the raw material and the exit of the products from the reaction zone, a very material fluctuation of temperature exists along the length of this zone and this often escapes the attention of the worker owing to the wrong location of the temperature measuring points. It was shown that in order to insure the isothermic conditions of the course of the reaction of cyclohexane dehydrogenation, the method of dilution of the catalyst with an inert diluent may be employed. Metallic aluminum was selected as such a diluent. The temperature established in this case corresponds to the recorded values.

The second problem which was subjected to a thorough study was that of the influence of the hydrodynamic regime on the reaction rate. During the realization of a chemical process which proceeds under real conditions, a considerable influence is exerted by the physical factors which are superimposed on the course of the main chemical reaction. Diffusion of the raw materials to the catalyst surface and the removal of the reaction products, the absorption or evolution of heat as well as the character of its propagation along the path of the reacting gas stream, not only affect the course of the chemical reaction but at times alter the latter. This problem has been analyzed more than once in the literature [2-6]. Nevertheless, the main attention of the investigators is usually directed to the study of the quality of the starting and the final products and of the catalyst properties, during the studies of processes which occur in the stream on heterogeneous catalysts. The problems of macrokinetics (hydrodynamics of streams, diffusion and heat transfer, etc.) are touched but lightly or are completely excluded, while it is specifically the accounting of the macroscopic factors that allow one to secure the true kinetic dependences of the chemical reactions proceeding under the real conditions.

It follows from the experimental data shown below, that the hydrodynamic regime of the process, along with the temperature regime, which affect the course of the process in any given region, actually determine the regularity and the value of the kinetic measurements that are obtained. It was shown that the transfer of the process under study to the exokinetic region may be accomplished by increased rates of flow of the reacting gas stream. This transfer is noted, under the conditions adopted for our experiments, upon reaching the linear velocity of 0.009-0.01 m/sec.

EXPERIMENTAL

The experiments were run in a flow installation, designed for work at high temperatures and pressures. The scheme of the installation is given in Fig. 1. The raw material was fed from burette 1 by means of a liquid pump 2 into reactor 3. Before entry into the reactor it was mixed in the mixing adapter with the hydrogen which entered through the precontactor 12 from the ballast tank connected to the hydrogen cylinder. The upper part of the reactor consisted of the heater and the feed evaporator. The heating of the reactor was accomplished by means of an aluminum furnace (block). The reactor had the internal diameter of 36 mm; two wells were located in the center (upper and lower wells) for locating the thermocouples. The internal diameter of the wells was 10 mm. Figure 1 shows the sites of temperature measurement in the reactor. The reaction products passed from the reactor into the condenser—cooler 4 and from this into the gas separator — receiver for high pressure 5, in which hydrogen was separated from the liquid product and led out of the system into the atmosphere through the rheometer and the gas meter 7. The liquid products were dropped into the low pressure receiver 6. We did not have any electrolytic hydrogen in the beginning of our work for which reason the precontactor 12 was installed in the setup, in which the hydrogen was purified by the removal of impurities through passage over the same catalyst at 450-480°. The setup was provided with a circulating gas pump 8, designed for circulating hydrogen during the reduction of the catalyst and for the heating and the cooling of the system.

The procedure of running the experiments was thus controlled.

1) The temperature was measured with chromel-alumel thermocouples connected to a portable potentiometer. The thermocouples were installed at the exit of the raw material mixture from the heating zone (in the upper well of the reactor; thermocouple No. 4) , in the beginning and the end of the catalyst layer (at the distance of 10 mm from the edge; thermocouples No. 1 and 3) and in the middle of the catalyst layer (in lower reactor well; thermocouple No. 2). 2) The pressure was measured with manometers located at reactor 3, the precontactor 12, the gas separator 15, the raw material pump 2 and the circulating pump 8. 3) The raw material feed was controlled by the liquid burette graduated to 0.2 ml. 4) The amount of hydrogen was measured at the exit from the setup by means of a graduated water rheometer and gas meter.

The molar ratio of the hydrocarbon and the hydrogen was calculated at the entry to the reactor. For this, the amount of hydrogen formed as the result of the reaction was substracted from the amount of gas leaving the setup, after adjustment to the normal conditions. The analysis of the catalyzates from the preliminary experiments showed that these consisted of benzene and unreacted cyclohexane. The decomposition was negligible. The bromine numbers of the catalyzates were 0-0.2. Therefore, the index of refraction was determined with the Abbe refractometer for all catalyzates and the molar or weight percent content of benzene contained in the catalyzate was found from the Pavlov table [7].
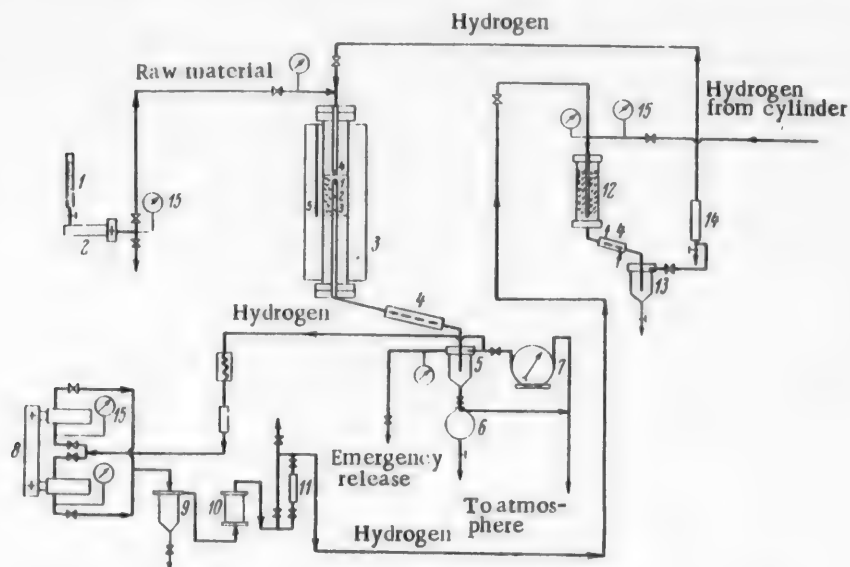
Fig. 1. Scheme of the installation. 1) Raw material burette; 2) raw material pump; 3) reactor; 4) cooler; 5) gas separator; 6) receiver; 7) gas meter; 8) circulating gas pump; 9) oil separator; 10) filter; 11) rotameter; 12) precontactor; 13) water separator; 14) drier; 15) manometer.

The cyclohexane used in the experiments was prepared by hydrogenation of benzene (analytically pure, d^{20}_4 0.8788, n^{20}D 1.5014) over a nickel catalyst. The completeness of the hydrogenation was determined by the formalite test. The resulting cyclohexane was distilled through a fractionating column, with 30-theoretical-plate efficiency and was characterized by the following constants: d^{20}_4 0.7780, n^{20}D 1.4262, b.p. 80.5°

Aluminoplatinum catalyst (Pt/Al$_2$O$_3$, promoted with halogen) in the form of small cylinders with height and diameter of 1.5-2 mm, was used in this work; the catalyst had been prepared in a sufficient quantity and had been reduced, under definite temperature conditions, with hydrogen.

Study of distribution of heat loads along the length of the catalyst layer. In order to make the conditions of the course of the reaction approximately isothermic, we used the method of dilution of the catalyst by an inert diluent, having selected metallic aluminum for this purpose. Other authors have used porcelain, glass or aluminum oxide for the dilution [8]. The aluminum was used in the form of pieces, the dimensions and the geometric form of which corresponded approximately to those of the catalyst grains. Passage of cyclohexane over pure aluminum showed that the aluminum remains inert under the conditions of the reaction: the product led from the system did not differ from the original cyclohexane; the composition of the entering and exiting hydrogen (from the system) also was the same. The catalyst was loaded into the reactor along with the diluent so that the concentration of the former in the diluent would be uniform through the entire height of the reaction zone.

Under the term "catalyst layer" we shall understand, in the following material, the meaning of the layer of the catalyst zone with the diluent, and in each separate case the amount of the catalyst and the degree of its dilution will be indicated, the dilution being measured by volume. The catalyst layer was placed at such a height in the reactor at which the temperature of the furnace heating the reactor (block) is constant. The

TABLE 1

Effect of Dilution of the Catalyst on the Temperature Regime in the Catalyst Zone (Pressure 20 atm.)

Conditions of experiments						Catalyzate	
Temperature in			space velocity (ml/ml of cat./hr)	feed of C_6H_{12} (moles/hr)	weight % of M_{H_2} : $M_{C_6H_{12}}$	n_D^{20}	weight % of benzene
start of layer	middle of layer	end of layer					
Dilution 1 : 10 •							
Charged: 2.5 ml of catalyst and 25 ml of diluent							
478°	467°	478°	19.2	0.445	11.2	1.4830	80.8
470	451	468	39.1	0.908	9.6	1.4650	59.4
470	441	458	61.2	1.420	9.1	1.4525	42.2
470	445	458	105.0	2.440	9.2	1.4439	29.7
Dilution 1 : 20							
Charged: 2.5 ml of catalyst and 50 ml of diluent							
470°	468°	471°	19.4	0.450	10.9	1.4796	76.6
473	468	474	40.5	0.940	9.1	1.4670	62.0
474	470	470	63.5	1.472	8.6	1.4574	49.0
475	469	470	80.6	1.765	9.3	1.4480	35.8
475	469	471	102.0	2.370	9.8	1.4495	38.0
Dilution 1 : 40							
Charged: 2.5 ml of catalyst and 100 ml of diluent							
470°	469°	471°	19.2	0.445	9.9	1.4876	86.0
470	471	472	39.1	0.903	9.7	1.4748	71.4
470	469	471	60.0	1.396	8.5	1.4655	60.0
468	468	470	102.0	2.370	7.6	1.4530	43.0
472	471	472	153.3	3.550	10.4	1.4408	24.8
Dilution 1 : 60							
Charged: 2.5 ml of catalyst and 150 ml of diluent							
471°	469°	471°	19.5	0.450	10.2	1.4850	83.0
470	473	472	41.2	0.955	9.4	1.4756	74.4
470	470	470	62.0	1.440	9.0	1.4658	60.2
469	479	469	105.0	2.440	8.7	1.4520	41.5

• The temperature of entry of the raw material mixture into the catalyst zone is taken to be the temperature in the "beginning of the layer", for this group of experiments.

regime of the experiment was considered as having been established when the desired feed rate of raw material and hydrogen was attained. The time at which two or three 15-minute samples of the catalyzate had the same index of refraction was taken to be the beginning of the experiment, after which the experiment was run for 1-2 hours longer. The given series of runs was performed under 20 atm pressure and at space velocity of the cyclohexane feed ranging from 20 to 150 milliliters/milliliter of catalyst per hour (considering the charged catalyst volume without the diluent) and at molar ratio of hydrogen to cyclohexane of 10:1. The amount of the catalyst was kept constant (2.5 ml or 1.2 g) and only the degree of its dilution was varied: 1:10, 1:20, 1:40 and 1:60. The conditions and the results of the experiments are given in Table 1.

The heights of the catalyst layers in the reactor, the differences in temperatures and the degrees of conversion of cyclohexane, depending on the dilution of the catalyst, are given in Table 2 and on Fig. 2. It is possible to conclude from these data that an approach to isothermic conditions of the reaction course occurs with increasing dilution of the catalyst: the temperature differences along the height of the catalyst layer become smaller as do those between the temperature of the heater furnace and the mean temperature inside the

catalyst layer. Not only does the catalyst dilution permit the approach to a uniform heat load distribution in the layer, but owing to the lengthening of the latter the heat exchange surface is increased, which brings about a rapid heat compensation, the heat being consumed in the endothermic reaction. The height of the catalyst layer in the reactor with 40- and 60-fold dilutions reaches 100 and 150 mm, the temperature over the entire layer becomes constant at all space velocities and, therefore, the maximum possible degree of conversion is

TABLE 2

Change of the Temperature Differences and of the Benzene Content in the Catalyzates Depending on the Degree of Dilution of the Catalyst

	Degree of dilution of the catalyst			
	1 : 10	1 : 20	1 : 40	1 : 60
Height of catalyst layer (in mm)	25	48	100	150
Difference in temperature between entry into the catalyst layer and the middle of the layer during feed of cyclohexane at (in ml/ml of catalyst per hour)				
40	19	5	<1—2	
60	29	4	<1—2	
100	25	6	<1—2	
Benzene content of the catalyzate (in wt.%) during feed of cyclohexane at (in ml/ml of catalyst per hour)				
40	59.4	62.0	71.4	72.4
60	42.2	49.0	60.0	60.2
100	29.7	38.0	43.0	41.5

established corresponding to the particular temperature, pressure and contact time. Therefore, the relationship found between the amount of the catalyst and the amount of the diluent assures the running of the reaction under isothermic conditions. Hence, the further study of the conversion of cyclohexane over the alumino-platinum catalyst was run with the dilution of the latter by 60-fold.

Fig. 2. Effect of dilution of the catalyst on the degree of conversion of cyclohexane. 1) 102-105 ml/ml of catalyst per hour; 2) 60 ml/ml of catalyst per hour; 3) 40 ml/ml of catalyst per hour.

Study of the effect of hydrodynamic and diffusional factors on the degree of conversion of cyclohexane. The following devices are usually employed in practice for finding the exokinetic region in running a reaction in a stream flow; 1) alteration of the length of the catalyst layer with the constant contact time, whereby the region is found in which the degree of conversion is independent of the layer length; 2) a number of reactors, with different diameters, is taken with a constant amount of the catalyst and the amount of raw material feed is varied with measurements necessary to determine the exokinetic region. In both cases the effect of alteration of the linear velocity of flow on the alteration of the degree of conversion is studied.

We used the first device. A series of experiments was set up with the amount of the catalyst being 0.5, 1.0, 1.7 and 2.5 ml (with 1 : 60 dilution)

and with 2.5 ml (dilution 1 : 40) at 470° and 20 atm pressure. The molar ratio of hydrogen to cyclohexane was maintained at 10 : 1. Each series of the experiments was run with a fresh portion of the catalyst from the same preparation batch. The catalyst stability was checked by control experiments. The conditions for running the experiments and the values of the linear velocity of the gas stream are given in Table 3. The mean value of the amount of hydrogen at the entry and the exit from the reactor was used for the calculation of the linear velocities.

It follows from the data in Table 3 and Figure 3, that the transfer of the reacting molecules from the gas stream to the catalyst surface depends on the character of the gas motion in the channels formed by the catalyst grain. At the constant contact time, the degree of conversion of cyclohexane increases with increase of

TABLE 3

Effect of Linear Velocity on Degree of Conversion (Temperature 470°, pressure 20 atm)

Conditions of the experiment			Catalyzate		Linear velocity (m/sec)
feed of C_6H_{12} (moles/hr)	molar ratio of $M_{H_2} : M_{C_6H_{12}}$	space velocity (ml/ml of catalyst/hr)	n_D^{20}	wt. % of benzene	
Charged: 0.5 ml of catalyst					
0.208	8.7	45.0	1.4550	45.8	0.0019
0.260	10.7	56.0	1.4510	40.0	0.0029
0.393	9.1	85.0	1.4460	32.7	0.0037
0.452	9.9	97.5	1.4432	28.2	0.0047
Charged: 1.0 ml of catalyst					
0.767	8.5	82.8	1.4540	44.6	0.0073
0.186	10.0	20.0	1.4735	70.0	0.0020
0.372	9.4	40.1	1.4623	55.8	0.0038
0.574	10.2	61.9	1.4570	48.5	0.0061
0.927	8.9	100.0	1.4520	41.6	0.0088
0.937	8.8	101.0	1.4508	39.8	0.0088
0.770	9.2	83.0	1.4528	42.8	0.0075
Charged: 1.7 ml of catalyst					
0.603	8.7	39.4	1.4740	70.6	0.0058
0.293	9.2	19.2	1.4339	82.0	0.0033
0.982	8.2	64.3	1.4660	60.6	0.0089
1.260	8.7	83.0	1.4590	51.3	0.0119
1.470	9.3	96.4	1.4535	43.5	0.0141
2.120	8.3	116.0	1.4504	39.5	0.0200
0.607	9.9	39.7	1.4710	66.8	0.0650
Charged: 2.5 ml of catalyst					
0.473	10.0	20.4	1.4854	83.5	0.0052
0.958	9.4	41.2	1.4756	72.4	0.0098
0.967	9.2	41.6	1.4743	70.9	0.0099
1.380	9.1	59.8	1.4690	64.2	0.0138
1.440	9.0	62.0	1.4658	60.2	0.0138
1.910	9.5	82.0	1.4575	48.8	0.0139
2.440	8.6	105.0	1.4520	41.5	0.0240
0.452	10.1	19.5	1.4850	83.0	0.0052
Charged: 2.5 ml of catalyst (dilution 1 : 40)					
0.455	9.9	19.4	1.4876	86.0	0.0049
0.906	9.7	39.1	1.4748	71.4	0.0096
1.390	8.5	60.0	1.4655	60.0	0.0130
2.240	8.9	96.7	1.4507	39.7	0.0230
2.370	7.6	102.4	1.4530	43.0	0.0197
3.550	10.5	153.0	1.4408	24.8	0.0377

the linear velocity. The dependence of the degree of conversion on the velocity of the gas stream indicates that the process is in the diffusional area; curves in Fig. 3 rise steeply upward. With further increase of the linear velocity, the degree of conversion of cyclohexane remains constant and independent of the linear velocity:
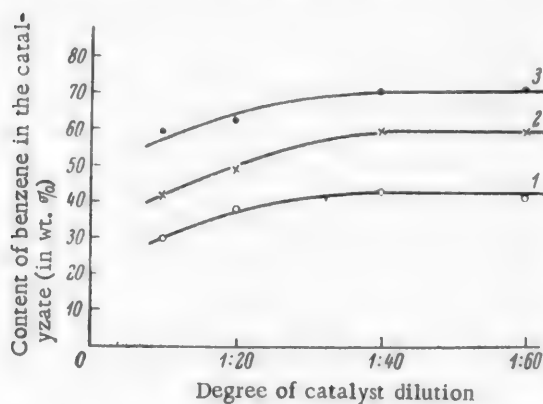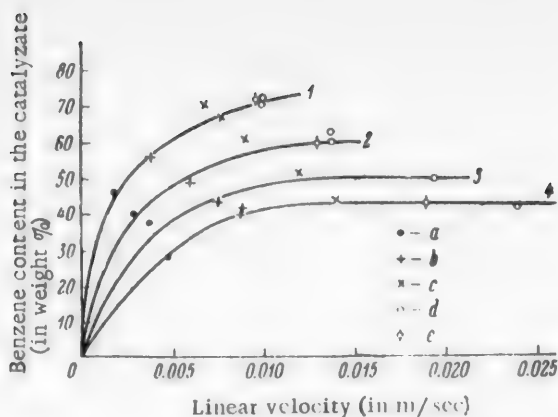
Fig. 3. Effect of the velocity of the gas stream on the degree of conversion of cyclohexane. 1) 40 ml/ml of catalyst per hour; 2) 60 ml/ml of catalyst per hour; 3) 80-90 ml/ml of catalyst per hour; 4) 100 ml/ml of catalyst per hour. Charged: amount of catalyst (in ml) — a) 0.5, b) 1.0, c) 0.7; d) 2.5, e) 2.5 (dilution 1 : 40).

the curves run parallel to the abscissa axis. This nature of the curves may be explained by the fact that under these condition used in the experiment exodiffusional and transitional regions occur up to the values of the linear velocity of 0.009-0.01 m/sec, while beginning with the value of linear velocity of about 0.01 m/sec and higher, the transition to the exokinetic region occurs, in which the observed rate of the chemical reaction coincides with the true rate of the chemical reaction on the catalyst surface.

SUMMARY

The conditions were found which permit one to run the reaction of dehydrogenation of cyclohexane over an aluminoplatinum catalyst under isothermic conditions and in the exokinetic region.

It was shown that it is possible to use the method of catalyst dilution with an inert diluent (specifically, metallic aluminum) at the proportion of 1 volume of catalyst per 40 or 60 volumes of the diluent in order to insure the isothermic conditions of the progress of the reaction.

The practical limits of the exodiffusional region were determined. It was shown that under the given experimental conditions, the reaction proceeds in the exokinetic region beginning with the magnitude of the linear veolcity of the stream equal to 0.009-0.01 m/sec.

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THE CONDENSATION OF O-NITROANISOLE WITH CHLORAL HYDRATE

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Nitrodiaryltrichloroethanes are frequently prepared by nitration of appropriate DDT analogs [1-7]. Among the direct syntheses of these compounds, the condensations of o- and p-nitrophenol [8, 9] and o-nitroanisole with chloral hydrate [10] are known. Shirley [10] obtained only 12% of 1,1,1-trichloro-2,2-di-(4-methoxy-3-nitrophenyl)-ethane (II) from o-nitroanisole (0.5 mole) and chloral hydrate (0.25 mole) in the presence of concentrated sulfuric acid (50 g) and 20% oleum (100 g). Shirley made no mention of the formation of any other substances in this condensation.

In examining the synthesis of trichlorinated carbinols and their reaction [11], we studied the condensation of o-nitroanisole with chloral hydrate under the action of concentrated sulfuric acid. By changing the amount of the latter and the rate of its addition, we obtained a 60% yield of substance (II) and a small amount (5%) of 1,1,1-trichloro-2,2-(4-methoxy-3-nitrophenyl)-(2'-methoxy-3'-nitrophenyl)-ethane (III) from o-nitroanisole (0.2 mole), chloral hydrate (0.1 mole) and sulfuric acid (1.5 mole). With a smaller amount of sulfuric acid (0.41 mole per 0.1 mole of o-nitroanisole) we were able to isolate a small amount (6%) of the intermediate 4-methoxy-3-nitrophenyltrichloromethylcarbinol (I). In some condensations of o-nitroanisole (0.2 mole) with chloral hydrate (0.1 mole) and sulfuric acid (1.5 mole) we obtained only traces of the trichlorinated carbinol (I) and the bulk of the mass formed substance (IV), which did not melt when heated to 350°. Its oxidation product gave a positive reaction for an anthraquinone nucleus. In analogy with the work of Quelet [12], we consider that substance (IV) is the self-condensation product of (I) – bis(mesotrichloromethyl)-dimethoxydinitro-dihydroanthracene.

All the reactions performed may be represented by the scheme on the following page.

EXPERIMENTAL

Condensation of o-Nitroanisole with Chloral Hydrate

Experiment 1. 150 g (1.5 mole) of concentrated sulfuric acid was added in separate portions over a period of 8 hours to a mixture of 30 g (0.2 mole) of o-nitroanisole, 16.5 g (0.11 mole) of chloral hydrate and 15 ml of dry chloroform. The mixture was stirred and its temperature kept at 15-17°. The addition of the sulfuric acid made the solution red. After standing overnight, the solution was decomposed with dilute alkali. The oil liberated was washed several times with water and steam distilled to remove solvent and unreacted o-nitroanisol (10 g) from it and leave a thick mass. Part of the oil was extracted with ether and from this we were able to obtain a small amount of a fraction with b.p. 190-195° (20-25 mm). On standing, this fraction changed into clear, amber yellow crystals with m.p. 110-111° (I).

Found %: C 35.50; H 2.52; Cl 35.48; N 4.71. $C_9H_8O_4NCl_3$. Calculated %: C 35.94; H 2.68; Cl 35.40; N 4.66.

4-Methoxy-3-nitrophenyltrichloromethylcarbinol (I) is not described in the literature. 2.5 g of concentrated sulfuric acid was slowly added to a mixture of 1 g of (I) and 0.5 g of o-nitroanisole. The mixture became red, gave off heat and, after some time, solidified. The mixture was decomposed with dilute alkali and

the precipitate washed with water. Recrystallization from benzene and methanol gave yellow crystals with m.p. 162-163°. The melting point of a mixture of them with substance (II) was not depressed.

Oxidation of (I) with chromium trioxide in acetic acid gave pale yellow crystals of 4-methoxy-3-nitro-ω,ω,ω-trichloroacetophenone (V). After recrystallization from benzene and petroleum ether, the substance had m.p. 92-93°. Alkaline decomposition of (V) [12, 13] gave 3-nitroanisic acid (VI) with m.p. 182-183°. According to literature data [14]: m.p. 186-187°.
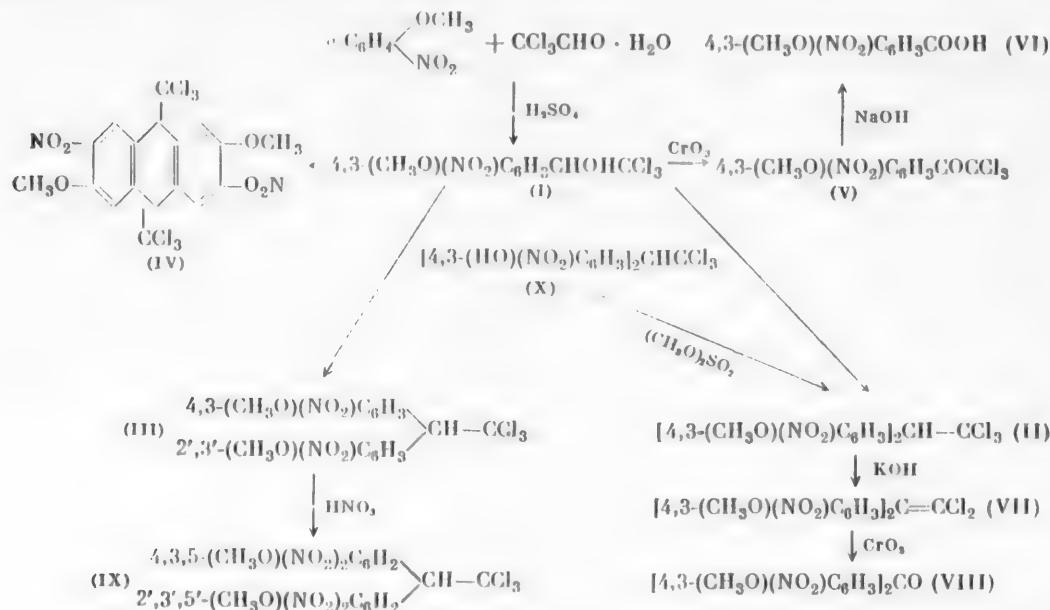
The ether-insoluble residue was treated with methanol several times. Dilution of the methanol solution with water precipitated claret colored substance (IV) (30 g), which was readily soluble in acetic acid, sparingly in methanol, ethanol and acetone and insoluble in ether, benzene, chloroform and petroleum ether. When heated to 350°, it did not melt.

Oxidation of (IV) [15] with potassium dichromate in sulfuric acid gave a flocculent precipitate, which gave a qualitative reaction for a compound containing an anthraquinone nucleus, after recrystallization from acetic acid.

Experiment 2. 15 g (0.1 mole) of o-nitroanisole, 8.2 g (0.05 mole) of chloral hydrate and 40 g (0.41 mole) of concentrated sulfuric acid, which was added to the mixture dropwise over a period of 8 hours, were worked up in the usual way to give a recovery of 8 g of o-nitroanisole and a yield of 1.8 g of an oil with b.p. 190-195° (20-25 mm), which solidified. The m.p. was 111° (from ether). The melting point of a mixture of this substance and similar crystals from experiment 1 was not depressed.

Experiment 3. The amounts of the starting materials were the same as in Experiment 1. The reaction was carried out without a solvent. The sulfuric acid was added dropwise over a period of 8 hours. The reaction temperature was kept at 15-17°. The decomposition and isolation of reaction products was as in experiment 1. After steam distillation of the o-nitroanisole, the viscous residue solidified. It was recrystallized from methyl alcohol with activated charcoal added and then from a mixture of benzene and methanol to give yellow crystals of (II) with m.p. 162-163°. The yield was 26 g (60%). 4 g of (II) was boiled for 12 hours with 1.6 g of sodium hydroxide in 20 ml of methyl alcohol. After evaporation of the alcohol and dilution with water, the reaction mixture gave a precipitate of 4,4'-dimethoxy-3,3'-dinitrophenyldichloroethylene (VII), which was recrystallized several times from benzene and then from a mixture of benzene and alcohol. The crystals had m.p. 157-158°. According to Shirley [10], the m.p. is 160-161°.

Oxidation of (VII) with chromium trioxide in acetic acid yielded 4,4'-dimethoxy-3,3'-dinitrobenzophenone (VIII) with m.p. 175-176° (from chloroform). According to literature data [10], the ketone melts at 178-180°.

1,1,1-Trichloro-2,2-di-(3-nitro-4-hydroxyphenyl)-ethane (X), obtained by condensation of o-nitrophenol with chloral hydrate [8], was methylated with dimethyl sulfate [17]. Dry sodium phenolate, obtained from 2 g (X) was treated with 10 ml of toluene and 4 ml of dimethyl sulfate. After being heated for 2 hours on a water bath and decomposed, the reaction product was extracted with benzene. We obtained pale yellow crystals with m.p. 162-163°. The melting point of these crystals was not depressed by admixture with (II).

The mother solution from experiment 3 deposited a small amount of lemon yellow crystals of (III) with m.p. 140°. Nitration of (III) [8] gave crystals with m.p. 175° (from a mixture of methyl alcohol and acetone). According to literature data [16], 1,1,1-trichloro-2(2'-methoxy-3',5'-dinitrophenyl)-2-(4-methoxy-3,5-dinitrophenyl)-ethane (IX) melts at 175-175.5°.

SUMMARY

1. Conditions were found for the condensation of o-nitroanisole with chloral hydrate in the presence of concentrated sulfuric acid, which gave a 60% yield of 1,1,1-trichloro-2,2-di-(4-methoxy-3-nitrophenyl)ethane. At the same time, a small amount (5%) of 1,1,1-trichloro-2-(4-methoxy-3-nitrophenyl)-2-(2'-methoxy-3'-nitrophenyl)-ethane was formed.

2. Previously unknown 4-methoxy-3-nitrophenyltrichloromethylcarbinol was isolated and characterized, having been found as an intermediate product in this condensation.

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ALKYLATION OF BENZENE WITH TETRAALKOXYSILANES

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The condensation of ethyl chloride and bromide with benzene in the presence of aluminum chloride gives a good yield of ethylbenzene if 0.1 mole of aluminum chloride is used with 1-1.5 mole of alkylating agent. With larger amounts of aluminum chloride, polyethylbenzenes are formed. These ratios are also optimal for the alkylation of benzene with other alkyl halides [1].

On alkylating benzene with ethyl bromide and benzyl bromide in the presence of catalytic amounts of aluminum chloride, prepared by Radziewanowski's method, the yields of ethylbenzene and diphenylmethane reached 70% and 63%, respectively [2].

The action of this catalyst was studied in detail by B. N. Dolgov, et al. [3], who established that with the use of 2% aluminum turnings, the yield of ethylbenzene reached 73%, the yield of isopropylbenzene, (from isopropyl chloride and benzene), 57% and the yield of tert-butylbenzene (from isobutyl chloride and benzene), 47%, while di- and triisopropylbenzenes and di- and tri-tert-butylbenzenes, respectively, were also formed. The yield of the monoalkylbenzenes fell with an increase in the molecular weight of the alkyl halide.

V. N. Azatyan used aluminum turnings (4%), without the introduction of hydrogen chloride from outside and obtained mainly monoalkylbenzenes in the alkylation of benzene with alkyl chlorides and bromides; using this method, he obtained an 80% yield of diphenylmethane from benzyl chloride and benzene [4].

In alkylating the benzene nucleus with ethyl esters of inorganic acids, Kane and Lowy [5] found that prolonged (25.5 hours) treatment of 0.25 mole of tetraethoxysilane in 624 g of benzene with 0.78 mole of aluminum chloride at 25-70° yielded ethylbenzene in 53% yield.

In the present work, we made a detailed study of the alkylation of benzene in the presence of aluminum chloride with various orthoesters of silicic acid (readily prepared by K. A. Andrianov's method [6]) and established that the result obtained depended on, a) the ratio tetraalkoxysilane : aluminum chloride, b) the degree of branching of the radical in the tetraalkoxysilane and c) the method by which the tetraalkoxysilane was prepared.

The experimental data presented in the table show that at a tetraalkoxysilane : aluminum chloride ratio of 1 : 4, we obtained ethylbenzene (in an alkylation with tetraethoxysilane) in 67.5% yield (Experiment 2), sec-butylbenzene (in an alkylation with tetrabutoxysilane) in 69% yield (Experiment 6) and tert-butylbenzene (in an alkylation with tetraisobutoxysilane) in 11% yield (Experiment 9), while with a ratio of 1 : 2, the yield of sec-butylbenzene reached 86.5% (Experiment 7), the yield of tert-butylbenzene, 44.5% (Experiment 10) and the yield of 2-methyl-3-phenylbutane (in the alkylation with tetraisoamyloxysilane was 44% (Experiment 11).

Experiments on the preparation of phenylcyclohexane (12), diphenylmethane (13) and 1,2-diphenylethane (14) at a ratio of 1 : 2 also gave better results as is shown in the table.

In the alkylation of benzene with tetrabutoxysilane in the presence of anhydrous ferric chloride (1 : 2), the yield of sec-butylbenzene was only 30%.

We alkylated benzene with tetraalkoxysilanes, prepared in a benzene medium and not purified and also isolated in a pure state. Under otherwise similar conditions, alkylation by the former gave higher yields of alkylbenzenes. The constants of the hydrocarbons obtained agree well with literature data.

A peculiarity of the alkylation of benzene with tetraalkoxysilanes is the fact that even with large amounts of aluminum chloride, monoalkylbenzenes are obtained and polyalkylbenzenes are practically absent from the reaction products.

The Raman spectra of the sec- and tert-butylbenzenes we obtained confirmed the purity of these preparations.

In the alkylation of benzene with tetraalkoxysilanes in the presence of aluminum chloride and ferric chloride, the same isomerization of the alkyl radical entering the benzene nucleus occurs, as occurs in alkylation with alkyl halides (and also olefins) and which was first described by G. G. Gustavson [7].

The results obtained in the present report confirm the mechanism which we proposed for the alkylation of benzene with tetraalkoxysilanes and which involves the formation of a complex of the tetraalkoxysilane with aluminum chloride (I), ionization of the complex with the formation of a reactive positive alkyl ion with its subsequent isomerization (II) and alkylation of the benzene nucleus by it (III), while the anion accepts the expelled proton to form a silicic acid and regenerates aluminum chloride.

$$\mathord{>}\!\!\mathord{\text-}SiOR + AlCl_3 \longrightarrow \left[\mathord{>}\!\!\mathord{\text-}Si\;O\!:\!AlCl_3 \atop \ddot{R} \right] \longrightarrow R^+ + \left[\mathord{>}\!\!\mathord{\text-}Si\;\underset{\cdot\cdot}{O}\!:\!AlCl_3 \right]^-$$
$$\text{(I)} \qquad\qquad\qquad\qquad \text{(II)}$$

$$ArH + R^+ + \left[\mathord{>}\!\!\mathord{\text-}Si\;\underset{\cdot\cdot}{O}\!:\!AlCl_3 \right]^- \longrightarrow Ar\!-\!R + \mathord{>}\!\!\mathord{\text-}SiOH + AlCl_3$$
$$\text{(III)}$$

$Ar = C_6H_5,\; C_{10}H_7;\; R = CH_3,\; C_2H_5,\; n\text{-}C_3H_7,\; iso\text{-}C_3H_7,\; n\text{-}C_4H_9,\; iso\text{-}C_4H_9,\; iso\text{-}C_5H_{11},\; C_5H_{11},\; C_6H_5CH_2,$
$C_6H_5CH_2CH_2.$
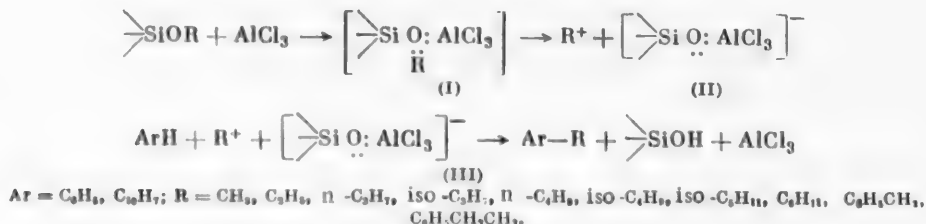
In the alkylation of naphthalene with tetraethoxysilane in a benzene medium in the presence of aluminum chloride, ethylbenzene (12%) is obtained together with α-ethylnaphthalene (24%).

EXPERIMENTAL

Alkylation of benzene in the presence of aluminum chloride. Into a three-necked, round-bottomed 500 ml flask with a reflux condenser, a dropping funnel and a stirrer, was placed 0.5 mole of alcohol and 150 ml of dry benzene and then 0.1 mole of silicon tetrachloride was added dropwise. The mixture was heated on a water bath, first at 70-80° and then at boiling point until the evolution of hydrogen chloride ceased (8-10 hours). The solution of tetraalkoxysilane was cooled to 20° and to it was added anhydrous aluminum chloride (0.2-0.4 mole) in small portions of 6-8 g (heat was produced and hydrogen chloride evolved). If the aluminum chloride did not dissolve completely, then the mixture was heated on a water bath to 50-60°. The reaction mixture was then heated as indicated above until the evolution of hydrogen chloride ceased, decomposed with ice water (150 g of ice + 100 ml of water) and distilled with superheated steam. The benzene layer was separated from the distillate, washed with soda and water, dried and boiled over sodium to remove alcohol. The precipitated alcoholate was filtered off and washed with benzene.

After removal of the benzene, the high-boiling residue was distilled over sodium from a flask with a fractionating head or on a fractionating column. The results obtained are given in the table.

The Raman spectra of sec- and tert-butylbenzene were plotted on the apparatus and by the method described by V. M. Tatevskii, et al.

The spectrum of sec-butylbenzene (Experiment 6) contained the frequencies ($\Delta \nu$ cm^{-1}): 312, 460, 620, 730, 750, 851, 947, 1000, 1030, 1094, 1160, 1188, 1210, 1340, 1462, 1614; and the spectrum of tert-butylbenzene, frequencies ($\Delta \nu$ cm^{-1}) 315, 344, 530, 614, 701, 837, 903, 929, 1000, 1029, 1114, 1158, 1194, 1263, 1445, 1462, 1600.

The Alkylation of Benzene with Tetraalkoxysilanes in the Presence of Aluminum Chloride

Expt. No.	Starting material					Substances obtained: their constants and yields					
	alcohols and alkoxysilanes									yield	
	name	am't (in g)	SiCl$_4$ (in g)	ben-zene (in ml)	AlCl$_3$ (in g)	name	boiling point (pressure in mm)	n_D^{20}	d_4^{20}	in g	in %
1	Methyl alcohol	16.0	17.0	250	26.7	Toluene	109—110°(754)	1.4958	0.8660	17.2	46.5
2	Ethyl alcohol	11.5	8.5	150	26.7	Ethylbenzene	135—137(754)	1.4958	0.8672	14.3	67.5
3	Tetraethoxysilane*	10.4	—	150	26.7		135—136.5(752)	1.4962	0.8665	12.7	60.0
4	n-Propyl alcohol	30.0	17.0	250	53.7	Isopropylbenzene	149.5—152(749)	1.4915	0.8622	24.1	50.0
5	Isopropyl alcohol	30.0	17.0	200	53.4		152—152.5(752)	1.4920	0.8625	22.3	46.5
6	n-Butyl alcohol	37.0	17.0	150	53.4	sec-Butylbenzene	172.5—173.2(748)	1.4896	0.8610	37.0	69.0
7	Tetrabutoxysilane**	37.0	17.0	150	26.7		172.5—173.5(754)	1.4896	0.8608	45.0	96.5
8	Tetrabutoxysilane**	16.0	—	200	26.7		172—173.5(754)	1.4898	0.8602	12.0	44.5
9	Isobutyl alcohol	37.0	17.0	250	53.4	tert-Butylbenzene	168—171(748)	1.4930	0.8678	5.8	11.0
10	Isoamyl alcohol	18.5	8.5	200	13.2	2-Methyl-3-phenylbutane	167—168.5(754)	1.4933	0.8676	11.9	44.5
11	Isoamyl alcohol	44.0	17.0	250	26.7		187.5—189(758)	1.4935	0.8760	26.0	44.0
12	Cyclohexenol	50.0	17.0	250	26.7	Phenylcyclohexane	124(26)	1.5252	0.9432	35.6	55.5
13	Benzyl alcohol	24.0	8.5	250	13.2	Diphenylmethane***	147(29)	—	—	14.0	41.5
14	β-Phenylethyl alcohol	61.0	17.0	300	26.7	1,2-Diphenylethane****	129—130(9)	—	—	40.0	58.0

*Tetraethoxysilane: b.p. 165-166° (756 mm) [6].

** Tetrabutoxysilane: b. p. 136° (7 mm) [6].

***Diphenylmethane: m. p. 26-26.5°.

****1,2-Diphenylethane: m. p. 51.5°.

All the frequencies belong to the compounds indicated and no impurities were indicated by the spectra.

Alkylation of benzene in the presence of ferric chloride. The tetrabutoxysilane obtained from 37 g of butyl alcohol and 17 g of silicon tetrachloride in 50 ml of dry benzene was diluted with 200 ml of dry benzene and 32.5 g of anhydrous ferric chloride added to it at $20°$ in portions of 8-9 g. The reaction mixture was worked up in the usual way to give 15.9 g (30%) of sec-butylbenzene with b.p. 172-173° (758 mm), n_D^{20} 1.400, d_4^{20} 0.8611.

Alkylation of naphthalene in the presence of aluminum chloride. To the tetraethoxysilane obtained from 19.5 g of anhydrous alcohol and 17 g of silicon tetrachloride in 50 ml of dry benzene was added 100 ml of dry benzene and 25.6 g of naphthalene dissolved in the solution. Then, with water cooling, 26.7 g of anhydrous aluminum chloride was added in 5-6 g portions. The reaction mixture was worked up appropriately to give 5 g of ethylbenzene with b.p. 135-136° (758 mm), n_D^{20} 1.4960, d_4^{20} 0.8668 and 7.4 g (24%) of α-ethylnaphthalene with b.p. 110-111° (8 mm), n_D^{20} 1.6052, d_4^{20} 1.013.

Literature data for α-ethylnaphthalene [8]: b.p. 112-116° (9 mm), n_D^{20} 1.6075, d_4^{20} 1.0123.

SUMMARY

The alkylation of benzene with tetraalkoxysilanes in the presence of aluminum chloride makes it possible to prepare good yields of monoalkylbenzenes without dialkylbenzenes.

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INVESTIGATION OF S-METHYLATED ARYLTHIOCARBAZONES

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In previous work [1, 2] we showed that the methylation of 1,5-diphenylthiocarbazone with methyl iodide in an alcoholic alkaline medium gave S-methylated derivatives in two forms, cis and trans, and established the rate of conversion of one form to the other, the activation energy and the effect of the nature of the solvents [3] and the electronic character of the substituents and their position in the phenyl nuclei on the ratio of the cis- and trans-forms obtained [2]. It seemed interesting to follow the effect of the nature of the substituents on the formation of cis- or trans-forms of methylated derivatives on a larger number of representatives.

S-Methyl Derivatives of Arylthiocarbazones of the General Formula $\begin{array}{c} RNH-N \\ RN=N \end{array}\!\!>\!C-SCH_3$

R	M. p.	Yield (in %)	Absorption max. (in mμ)	Empirical formula	Nitrogen content (in %) calc.	found
2-CH₃, CH₃ phenyl	130°	48	565	$C_{18}H_{22}N_4S$	17.18	17.33, 17.23
CH₃, CH₃ phenyl	125	48	568	$C_{18}H_{22}N_4S$	17.18	17.29, 17.21
OCH₃ phenyl	147	96	437	$C_{16}H_{18}O_2N_4S$	16.97	17.10, 17.07
CH₃O phenyl	145	67	438	$C_{16}H_{18}O_2N_4S$	16.97	16.83, 16.94
SCH₃ phenyl	139	48	448	$C_{16}H_{18}N_4S_3$	15.47	15.50, 15.58
Cl phenyl	151	48	560	$C_{14}H_{12}N_4Cl_2S$	16.52	16.07, 15.99
Br phenyl	164	97	425	$C_{14}H_{12}N_4Br_2S$	13.08	13.19, 13.15
Br phenyl	154	73	558	$C_{14}H_{12}N_4Br_2S$	13.08	13.50, 13.58
Br, CH₃ phenyl	174	48	573	$C_{16}H_{16}N_4Br_2S$	12.23	11.95, 11.90
CF₃S phenyl	114	49	558	$C_{16}H_{12}N_4F_6S_3$	11.91	12.50, 12.32

The S-methyl derivatives were synthesized in the following way: equimolecular amounts of arylthiocarbazones and methyl iodide were mixed in the cold in an alcoholic alkaline medium (sufficient alkali was taken to form the sodium salt of the thiocarbazone) and the mixture was left overnight. The methyl derivatives, which precipitated in well-formed crystals, were filtered off and washed with a small amount of water, alcohol and ether. After being dried in vacuum, the substances were analyzed and their absorption spectra examined. Some of the products obtained were also chromatographed on aluminum oxide columns [3]. The S-methyl derivatives of arylthiocarbazones synthesized are described in the table.

As the data in the table show, the S-methyl derivatives of arylthiocarbazones were obtained in good yields. All the preparations had only one absorption maximum. As was shown previously [1], S-methyl derivatives of arylthiocarbazones with an absorption maximum in the short-wave region of 420-470 mμ are cis-isomers; compounds with an absorption maximum in the region 530-570 mμ are trans-isomers.

The spectrophotometric data for ten different substituted S-methyl derivatives of 1,5-arylthiocarbazones, presented in the table, and for three S-methyl derivatives, which we examined previously [1], show that five of them with ortho-substituents give cis-derivatives, while compounds with substituents in the para-position give trans-derivatives.
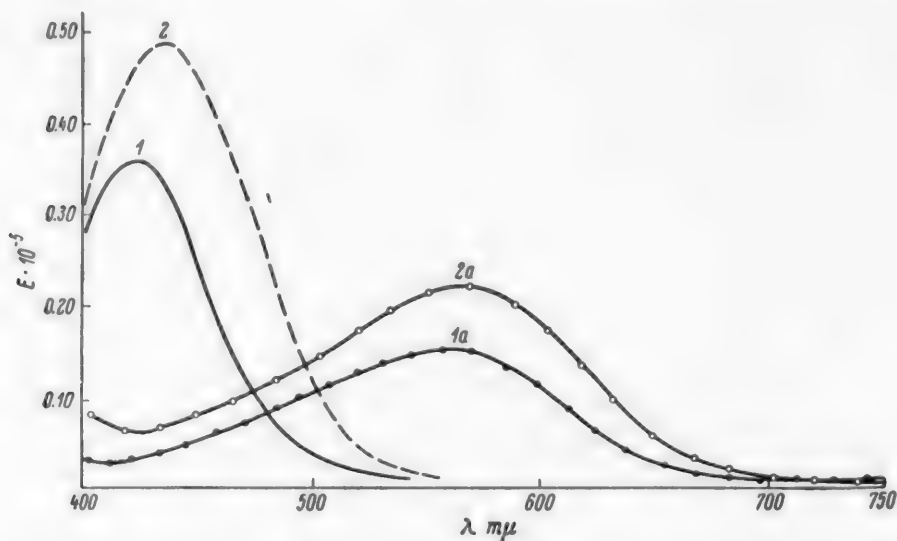
Absorption curves of S-methyl derivatives of 1,5-di-(2-bromo-phenyl)-thiocarbazone [cis-form (1) and trans-form (1a)] and 1,5-di-(2-anisyl)-thiocarbazone [cis-form (2) and trans-form (2a)].

As we showed previously [2, 3], under the action of diffuse sunlight, the cis-isomers are rapidly isomerized into the trans-forms. The figure shows the absorption curves of the cis-forms of the S-methyl derivatives of 1,5-di-(2-bromophenyl)- and 1,5-di-(2-anisyl)-thiocarbazones and their absorption curves after they had stood in diffuse sunlight for 30 minutes. The absorption curves of all the preparations were measured on an SF-2 spectrophotometer in benzene solution at a concentration $6.6 \cdot 10^{-5}$ M.

SUMMARY

Ten new S-methyl derivatives of various substituted 1,5-diphenylthiocarbazones were synthesized and their absorption spectra investigated.

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CATALYTIC CONVERSIONS OF PIPERIDINE IN A HYDROGEN
ATMOSPHERE

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The catalytic dehydrogenation of piperidine was first studied by Zelinskii and Borisov [1]. The authors found that platinized or palladized asbestos dehydrogenated more than 50% of the piperidine into pyridine at 250° in a single pass over the catalyst. Later a series of works [2-4] were devoted to the study of the dehydrogenation of substituted piperidine and bicyclic systems with piperidine rings over platinized or palladized asbestos and also on platinized charcoal. Terent'ev and Gurvich [5] investigated this reaction in the presence of palladized asbestos at 250° and came to the conclusion that the dehydrogenation of piperidine was accompanied by the formation of not only pyridine, but also a partial dehydrogenation product. The authors considered that tetrahydropyridine is probably this product and that its yield is about 20%. The dehydrogenation of N-methylpiperidine proceeds with elimination of the methyl group and the catalyzate also contains partial dehydrogenation products.

In the present work, we set out to examine the possibility of hydrogenolyzing piperidine in a flow system over a skeletal nickel-aluminum catalyst with the formation of 1-aminopentane by the scheme.

$$\underset{\overset{\displaystyle H_2C \quad CH_2}{\underset{\displaystyle NH}{H_2C \quad CH_2}}}{CH_2} \xrightarrow[Ni-Al]{H_2} CH_3-CH_2-CH_2-CH_2-CH_2-NH_2$$
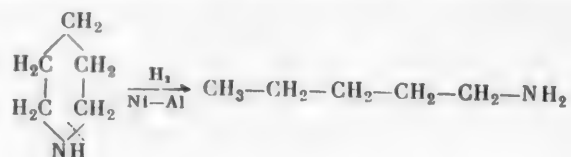
With this aim, we performed experiments on the hydrogenolysis of the piperidine ring at 250, 300, 350 and 400° and also over a copper-chromium catalyst at 400°.

As a result of an examination of the catalyzates, it was established that at elevated temperatures up to 400° over the skeletal nickel-aluminum catalyst, there was mainly destruction of the piperidine ring with the formation of a large amount of gaseous products, while at the same temperature, the copper-chromium catalyst produced quite a smooth dehydrogenation of piperidine into pyridine. A noticeable phenomenon was the formation of considerable amounts of α-picoline in all cases in the presence of nickel-aluminum catalyst and the content of it in a catalyzate from an experiment at 300° reached 12.6%. On the basis of this fact, we can put forward the proposition that under the given conditions methylene radicals arise on the surface of the nickel-aluminum catalyst and these methylate the pyridine formed into α-picoline.

$$\underset{\overset{\displaystyle H_2C \quad CH_2}{\underset{\displaystyle NH}{H_2C \quad CH_2}}}{CH_2} \longrightarrow \begin{array}{l} 3H_2 + \overset{\displaystyle \bigcirc}{N} \\[4pt] \underset{Ni}{|} \quad \underset{Ni}{|} \\ CH_2; \quad CH_2 + H_2 \rightarrow CH_4 \\ \underset{Ni}{|} \quad \underset{Ni}{|} \end{array}$$

$$\text{(pyridine)} + CH_2 \xrightarrow[\;Ni\;]{\;Ni\;} \text{(2-methylpyridine)} - CH_3$$
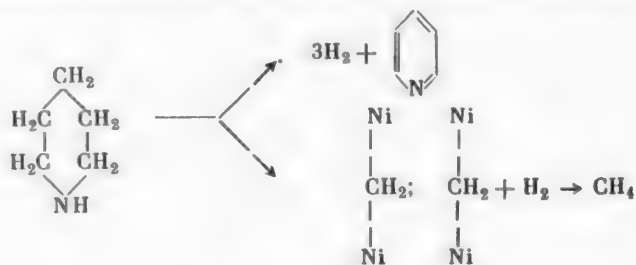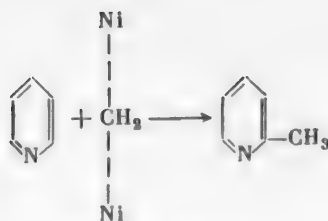
EXPERIMENTAL

The conversion of piperidine was studied in a flow system over skeletal nickel-aluminum catalyst at temperatures of 250, 300, 350 and 400° with a volume rate of 0.2 hour^{-1} and over a copper-chromium catalyst at 400° with a volume rate of 0.1 hour^{-1} in excess hydrogen. The skeletal nickel-aluminum catalyst was prepared by the method described previously by one of us [6] and the copper-chromium catalyst by Adkins' method [7].

The activity of the catalyst was determined from the change in refractive index of piperidine, when passed over the catalyst once. The starting piperidine had the following properties: b.p. 105° (739 mm), n_D^{20} 1.4535 and d_4^{20} 0.8642. The experimental conditions and the properties of the catalysts are given in Table 1.

TABLE 1

Experimental Conditions

Expt. No.	Catalyst	Temp.	Volume rate (in hour^{-1})	Am't of substance taken for expt (in g)	Yield of liquid catalyzate in		n_D^{20} of catalyzate
					r	%	
1		250°	0.2	200	175	87.5	1.4690
2	Nickel-aluminum	300	0.2	100	65	65.0	1.4725
3		350	0.2	100	51	51.5	1.4670
4		400	0.2	100	29	29.3	1.4940
5	Copper-chromium	400	0.1	145	125	86.0	1.4990

The liquid catalyzate was dried with fused potash and distilled on a column with an efficiency of 42 theoretical plates. An examination was made of fractions, which were either individual compounds or azeotropic mixtures of them according to their distillation curves. The properties of the catalyzates in fractions are given in Tables 2 and 3.

Fraction 2 (90-92°) was an azeotropic mixture of piperidine and water. Pure piperidine was isolated by treating this fraction with metallic sodium.

Fraction 4 (104-106°) consisted of unreacted piperidine.

Fraction 6 (113-115°) consisted mainly of pyridine, judging by its physical properties and the melting point of its picrate.

Fraction 8 (127-128°) was α-picoline.

Fractions 9-11 were isolated by distillation of the residue from a flask with a fractionating head.

Fraction 10 with b.p. 185-210° (the bulk boiling in the range 200-205°) probably contained N-cyclopentylpiperidine, judging by its properties [8].

As a comparison of the properties shows, the fractions with b.p. 105-106°, 113-115° and 127-129° are completely analogous to fractions 4, 6 and 8 in Table 2. In experiments at 350 and 400°, the yield of liquid catalyzate fell sharply due to the predominance of processes destroying the piperidine ring with the formation of considerable amounts of gaseous hydrocarbons, consisting of 50% methane and 50% ethane. Unreacted

TABLE 2

Properties of Fractions Obtained in the Catalysis of Piperidine Over a Nickel-Aluminum Catalyst at 250°

| Fraction No. | B. p. (at 730 mm) | Amount | | n_D^{20} | d_4^{20} | M. p. of picrates |
		in g	in % of catalyzate			
1	59—90°	4.0	2.3	1.4150	—	—
2	90—92	12.6	7.2	1.4310	0.9812	150°
3	92—104	1.2	0.7	1.4525	—	—
4	104—106	88.2	50.5	1.4573	0.8700	150
5	106—113	5.8	3.3	1.4710	—	—
6	113—115	14.7	8.4	1.4990	0.9772	164—165
7	115—127	3.2	1.8	1.4950	—	—
8	127—128	14.8	8.5	1.4990	0.9462	164
9	128—185	7.0	4.0	1.4790	—	—
10	185—210	4.2	2.4	1.4760	0.8950	167—168
11	210—250	3.5	2.0	1.5010	—	—
	Residue	13.2	7.5	—	—	—

TABLE 3

Properties of Fractions Obtained in the Conversions of Piperidine Over a Nickel-Aluminum Catalyst at 300°

| Fraction No. | B. p. (at 749 mm) | Amount | | n_D^{20} | d_4^{20} | M. p. of picrates |
		in g	in % of catalyzate			
1	88—105°	2.0	3.2	1.4310	—	—
2	105—106	36.8	56.7	1.4585	0.8683	150°
3	106—113	3.0	3.5	1.4740	—	—
4	113—115	6.5	10.0	1.5010	0.9780	164
5	115—127	1.9	3.1	1.4990	—	—
6	127—129	8.2	12.6	1.4985	0.9397	164—165
7	129—177	3.1	4.8	1.4900	—	—
	Residue	2.7	4.2	—	—	—

TABLE 4

Properties of Fractions Obtained in the Conversions of Piperidine Over a Copper-Chromium Catalyst at 400°

| Fraction No. | B. p. (at 737 mm) | Amount | | n_D^{20} | d_4^{20} | M. p. of picrates |
		in g	in % of catalyzate			
1	57—91°	3.8	3.0	1.3810	—	—
2	91—93	4.5	3.6	1.4290	0.9253	150°
3	93—104	2.8	2.3	1.4540	—	—
4	104—106	13.8	11.2	1.4560	0.8686	150
5	106—113	3.9	3.2	1.4870	—	—
6	113—115	65.9	53.2	1.5060	0.9859	164
7	115—150	9.1	7.5	1.4675	—	—
8	150—325	14.5	11.6	1.5120	—	—
	Residue	3.0	2.5	—	—	—

piperidine (82 and 50% respectively, calculated on catalyzate) was isolated from the liquid catalyzate. It was not possible to isolate individual compounds from the mixture of products boiling in the range 106 to 250-290° and forming 8-10% of the catalyzate. This mixture was probably condensation products of pyridine or piperidine with various alkyl residues, arising during the destruction of the piperidine ring.

The results of piperidine conversions on a copper-chromium catalyst are presented in Table 4.

The properties of the fractions 91-93°, 104-106° and 113-115° are also quite close to those of fractions 2, 4, and 6 (Table 2). As in the case of catalysis with a skeletal nickel-aluminum catalyst at 250-300°, the main product of piperidine conversions on a copper-chromium catalyst was also pyridine. In this case the hydrogenolysis of the piperidine ring with the formation of 1-aminopentane did not occur. It is noticeable that in the presence of the two catalysts there was very little hydrogenolysis of the piperidine molecule to give liquid products. Destruction tends predominantly toward gas formation. Apparently, these fragments arising on the catalyst surface produce alkylation of the pyridine formed to give alkyl derivatives, in particular, α-picoline.

SUMMARY

1. At 250 and 300° over a nickel-aluminum catalyst in a hydrogen atmosphere the predominant reaction of piperidine is dehydrogenation with the formation of pyridine and the simultaneous methylation of the pyridine formed to α-picoline by methylene radicals produced on the catalyst surface.

2. When the temperature is raised to 400°, there is much destruction of the material with the formation of gaseous hydrocarbons over a nickel-aluminum catalyst, in addition to the dehydrogenation of piperidine to pyridine.

3. It was shown that a copper-chromium catalyst at 400° actively dehydrogenated piperidine into pyridine.

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HYDROGENATION OF FURAN COMPOUNDS OVER A Ni-ZnO CATALYST

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The hydrogenation of furan derivatives, especially those with an unsaturated bond in the side chain, is of interest from the point of view of the possibility of selectively reducing such compounds. In general, the final hydrogenation products of furan compounds are paraffinic hydrocarbons and water. However, it was found to be possible to choose appropriate conditions for stopping the reaction at one of the intermediate stages and thus obtain products with various degrees of saturation. The most essential factors in the selective hydrogenation are the nature of the catalyst and the temperature. A large number of investigations have been devoted to a search for conditions for selectively hydrogenating the double bonds in the furan ring with the retention of the ether bonds. The most effective catalysts for this purpose were metals of group VIII of the periodic system: platinum, palladium, nickel, osmium and some others. However, for all these catalysts these is a definite maximum temperature, specific for each of them, above which, hydrogenolysis of the furan ring begins to predominate. Thus, on platinum promoted with iron salts, it is possible to hydrogenate various furan derivatives (furfural, pyromucic acid, furalacetone, etc.) into tetrahydrofuran derivatives in good very yields at normal temperatures in the liquid phase [1]. Hydrogenolysis of the furan ring occupies a subordinate position under these conditions. Meanwhile, in the hydrogenation of furan homologs over platinized charcoal in the gas phase at 275°, there is only hydrogenolysis of the furan ring at the C-O bond, which is not adjacent to the alkyl radical, and aliphatic ketones are formed in yields up to 95% [2]. The temperature range over which palladium behaves as a specific catalyst for the hydrogenation of the double bonds in the furan ring is extremely large. In the liquid phase at normal temperature [3] and in the vapor phase at 150° [4], the furan ring is hydrogenated without noticeable rupture. Even at 275°, the degree of hydrogenolysis of the furan ring at the C-O bond (1-5) is only about 25% over palladized charcoal [5].

Nickel catalysts show a wide variety of properties. Like palladium, they are extremely efficient in the hydrogenation of the furan ring. However, in contrast to palladium, the temperature range over which this reaction is the predominating one is very limited with nickel catalysts. In the liquid phase, alkyl and alkenyl derivatives of furan are hydrogenated to the corresponding alkyltetrahydrofurans in high yields at 100-118° over Raney nickel [6]. At temperatures not exceeding 100-140°, homologs of furan are hydrogenated smoothly in the vapor phase over nickel catalysts [7].

Wilson [8] found that the hydrogenation of sylvan over a nickel catalyst in the vapor phase gave an 86% yield of tetrahydrosylvan at 100° or at 75% yield of pentanone-2 at 185°.

Skeletal Ni-Al catalysts, similar to those investigated by us [9] in the hydrogenation of a series of alkyl- and alkenyl derivatives of furan at various temperatures, possess the extremely interesting capacity for producing so-called " conjugated" hydrogenolysis, in which the furan ring is cleaved both at the 1-5 C-O bond and at the 3-4 or 4-5 C-C bond. The rupture of the carbon-carbon bonds is accompanied by the simultaneous cleavage of the ether bond at 1-5, which leads to the formation of a molecule of a hydrocarbon and a molecule of an aliphatic alcohol or ketone from the alkylfuran molecule.

Rupture of the 1-5 bond
$$CH_3CH_2CH_2 - \underset{\underset{O}{\|}}{C} - R$$

Rupture of the 1-5
and 4-5 bonds
$$CH_3CH_2 - \underset{\underset{O}{\|}}{C} - R + C_nH_{2n+2}$$

Rupture of the 1-5
and 3-4 bonds
$$CH_3 - \underset{\underset{O}{\|}}{C} - R + C_nH_{2n+2}$$
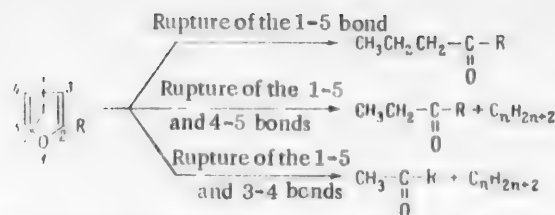
The furan ring in α-alkylfurans is hydrogenolyzed completely in the three given directions over a skeletal Ni-Al catalyst at even 235°. The temperature of 130-150° is the limit above which the hydrogenolysis reaction becomes predominant. Hence, it follows that homologs of furan boiling above this temperature cannot be hydrogenated smoothly into the corresponding alkyltetrahydrofurans over a skeletal Ni-Al catalyst in the vapor phase. The capacity of a skeletal Ni-Al catalyst to produce "conjugated" hydrogenolysis is a property specific to it. On nickel, deposited on aluminum oxide, hydrogenolysis of the furan ring with the formation of ketones proceeds to an insignificant extent (not more than 15%) and is accompanied by extensive decomposition of the furan ring [5].

All these data indicate that the properties of nickel catalysts depend most essentially on the nature of the carrier. The results of the present investigation confirm this conclusion. We found that in hydrogenation in the vapor phase, nickel deposited on zinc oxide was capable of hydrogenating the double bond in the side chain of an α-alkenylfuran or at higher temperatures, of hydrogenolyzing the furan ring exclusively at the C-O bond, not adjacent to the alkyl radical. This catalyst is not capable of hydrogenating multiple bonds of the furan ring in the vapor phase. Thus sylvan remains unchanged when it is passed over an Ni-ZnO catalyst at 140° Under the same conditions, α-propenylfuran is hydrogenated to α-propylfuran in almost quantitative yield.

$$\text{(furan)} - CH = CHCH_3 \xrightarrow[140°]{H_2,\ Ni-ZnO} \text{(furan)} - CH_2CH_2CH_3$$
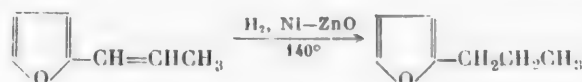
The hydrogenation of sylvan and α-ethyl- and α-propylfurans at 250° proceeded with complete opening of the ring at the 1-5 C-O bond and the formation of pentanone-2, hexanone-3 and heptanone-4, respectively, in yields of up to 95%.

$$\text{(furan-R)} \xrightarrow[250°]{H_2,\ Ni-ZnO} CH_3CH_2CH_2 - \underset{\underset{O}{\|}}{C} - R$$

$$R = CH_3,\ C_2H_5,\ n\text{-}C_3H_7.$$
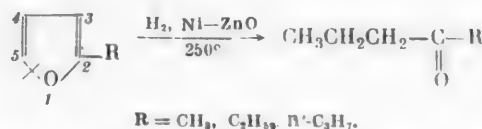
Thus, depending on the temperature, the Ni-ZnO catalyst may produce one of two reactions with a high degree of selectivity: hydrogenation of a double bond in the side chain without touching the furan ring or hydrogenolysis of the ring at the 1-5 C-O bond with the simultaneous or subsequent hydrogenation of the double bonds of the ring.

We should note that it is impossible to achieve selective hydrogenation of the double bond in the side chain in the vapor phase over other nickel catalysts (Raney nickel and nickel on kieselguhr) since there is always hydrogenation of the furan ring with them. With respect to its capacity for cleaving the furan ring exclusively at the 1-5 C-O bond (and moreover, in high yields), nickel on zinc oxide is similar to platinized charcoal [2] and differs sharply from the skeletal nickel-aluminum catalyst, which still remains the only one capable of "conjugated" hydrogenolysis of the furan ring.

EXPERIMENTAL

Catalyst. The nickel on zinc oxide on zinc oxide, containing 30% of finely dispersed nickel, was prepared by coprecipitation of zinc and nickel hydroxides from a solution of their nitrates with ammonia. The

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precipitate was washed with water until the nitrate ion disappeared (reaction with diphenylamine), filtered off, dried at 120° and formed into small cylinders. After this, the catalyst was placed in a silica reaction tube and reduced with hydrogen. The most active samples of catalyst were obtained when the following temperature conditions were observed: for the first 4 hours, the catalyst was reduced at 200°, for the following 4 hours at 250° and finally for a further 4 hours at 300°. In each experiment, 100 ml of catalyst was used.

Starting materials. α-Ethyl- and α-propylfurans were prepared by direct hydrogenation of methyl- and ethylfuranyl carbinols over palladized charcoal at 200-230° in yields of 70-80% [10].

$$R = CH_3, \ C_2H_5.$$
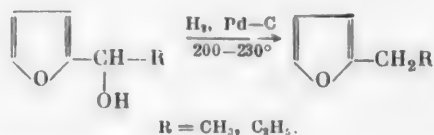
α-Propenylfuran was prepared together with small amounts of α-propylfuran in the dehydrogenation of ethylfurylcarbinol on aluminum oxide at 350°. Pure sylvan was isolated from the techical product by distillation on an efficient column. The physical properties of the alkyl- and alkenylfurans obtained, after their distillation on an efficient column, are presented in the table.

Properties of Starting Alkyl- and Alkenylfurans

Starting material	Boiling point (pressure in mm)	d^{20}_4	$n^{20}D$
Sylvan	63-64° (750)	0.9120	1.4321
α-Ethylfuran	91-91.5° (750)	0.9018	1.4402
α-Propylfuran	114-115 (745)	0.8876	1.4395
α-Propenylfuran	132-133 (752)	0.9457	1.5098

We used 100 g of each compound for the investigation. The starting material was introduced into the reaction zone at a volume rate of $0.1 \ \text{hour}^{-1}$. The hydrogenation was carried out at two temperatures: 140 and 250°. The catalyzates obtained were dried over calcium chloride and fractionated on a column with an efficiency of 40 theoretical plates.

The sylvan was unchanged at 140°, while α-propenylfuran was practically quantitatively hydrogenated to α-propylfuran at this temperature. As a result of hydrogenating sylvan and α-ethyl- and α-propylfurans at 250°, we obtained up to 95% yields of the corresponding aliphatic ketones – the products of hydrogenolysis of the furan ring at the 1 – 5 C – O bond.

1. Pentanone-2, b. p. 101-102° (755 mm), d^{20}_4 0.8086, $n^{20}D$ 1.3906. Semicarbazone, m. p. 109-110°.

2. Hexanone-3, b. p. 123-124° (755 mm), d^{20}_4 0.8165, $n^{20}D$ 1.4002. Semicarbazone, m. p. 110-110.5°

3. Heptanone-4, b. p. 142.5-143° (755 mm), d^{20}_4 0.8170, $n^{20}D$ 1.4082. Semicarbazone, m. p. 132.

SUMMARY

1. Nickel deposited on zinc oxide is incapable to hydrogenating the furan ring in the vapor phase.

2. Depending on the temperature, an Ni-ZnO catalyst can selectively hydrogenate the olefin bond in the side chain of alkenylfurans (almost quantitatively at 140°) or hydrogenolyze the furan ring at the C-O bond not adjacent to the alkyl radical, and in the latter case, the corresponding aliphatic ketones are formed in up to 95% yields (or theoretical) at 250°.

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A CONTRIBUTION ON THE STRUCTURE OF CITRAL, OBTAINED
FROM SYNTHETIC GERANYL CHLORIDE

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As a result of a systematic study of the telomerization of diene hydrocarbons with halogen derivatives begun in our laboratory [1-3], K. V. Lééts and A. K. Shumeiko et al., were able to synthesize citral from isoprene [4]. The question naturally arose as to whether this citral differed from natural samples and especially from the citral obtained on an industrial scale from coriander oil.

According to literature data [5-7], the citral obtained from natural sources, for example lemongrass oil, consists predominantly of citral "a", geranial, and in synthetic citral, neral (citral "b") predominates [8]. To a greater or lesser extent, a series of investigators have been able to separate the geometrical isomer of citral [6-8] and the infrared spectra of the two isomers have been examined. The infrared spectra were also most convenient for determing the structure of synthetic citral from isoprene, the more so since it would be possible to solve the problem of the α- and β-form content simultaneously [9].

We examined the infrared spectra of two samples of synthetic citral, obtained by the Sommelet reaction from the mixture of terpene chlorides, formed in the telomerization of isoprene with its two hydrochlorides: prenyl chloride (1-chloro-3-methylbutene-2) and dimethylvinylchloromethane (2-chloro-2-methylbutene-3) [4, 10].

The spectra obtained were very similar to each other. Thus, it was again shown that in a telomerization with isoprene, the two hydrochlorides of isoprene form mixtures of telomers with similar compositions (Fig. 1, curves 5 and 6). Further, these spectra showed that the synthetic citral, like the natural one, contained both possible geometrical isomers, since the spectra of both samples of synthetic citral contained the frequencies specific for geranial (820, 868, 892 cm^{-1}) and for neral (1154 and 843 cm^{-1}); moreover, judging by the intensities, geranial predominated, as in natural samples.

However, the spectra of synthetic citral in the region 800-900 cm^{-1} differed slightly from the spectra of natural citral, obtained from coriander oil. In this region they were more similar to the spectrum of citral "a", i.e., geranial.

Besides the normal frequencies for natural citral, a frequency of 1252 cm^{-1} was quite clearly expressed in the spectrum of synthetic citral.

Thus, it was established that synthetic citral was not completely identical with the natural one and apparently contained a large amount of geranial and an impurity, characterized by the frequency 1252 cm^{-1}.

An examination of the Raman spectra of synthetic and normal citral led to the same conclusion. Samples of synthetic citral, obtained from the two isoprene hydrochlorides, had practically identical spectra. At the same time, these spectra differed from the spectrum of normal citral. As in the infrared spectra, a weak frequency at 1240 cm^{-1} was observed here, but was absent from the spectra of citral from natural sources [11]. In addition, there were differences in the intensities of the bands at 1189 and 1278 cm^{-1}. The frequencies of the conjugated system in the spectra of all the samples differed neither in position nor in intensity (1630 and 1670 cm^{-1}).

We then examined the ultraviolet spectra of normal and synthetic citral. They hardly differed from each other in the position of the two characteristic maxima of citral [12] (235 and 315 mμ), but these maxima had different intensities. The synthetic citral absorbed more strongly in the region of the K-maximum and less strongly in the region of the R-maximum. The geometrical isomers usually differ in this way with the K-band normally more intense in spectra of the trans-isomers [13].
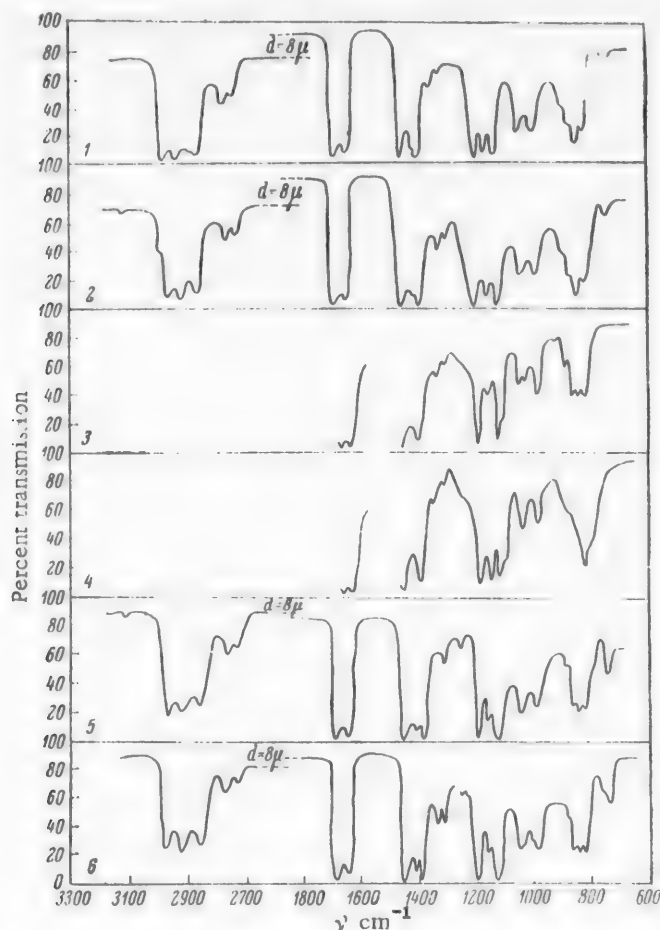
Fig. 1. Infrared transmission spectra of various citral samples.
1) Technical, 2) prepared by oxidation of pure geraniol, 3) ger-
anial "a", 4) neral "b", 5) prepared from the 1,2-hydrochloride
of isoprene, 6) prepared from the 1,4-hydrochloride of isoprene.

Thus, the ultraviolet spectra also indicate that normal and synthetic citral apparently differ in the contents of the geometrical isomers.

Starting from the data obtained, it was natural to attempt to separate synthetic citral into geometric isomers in order to determine each of them quantitatively. However, work in this direction led to the conclusion that the methods described in the literature are not reliable. We are continuing work in this direction.

In parallel with determining the geometric configuration of synthetic citral, we also examined the possibility of it containing a terpineol α-form. For this purpose we examined the infrared spectrum of all the citral samples in the region of 6100 cm^{-1}. It is known that only compounds containing a $CH_2=$ grouping absorb in this region [14]. The investigation showed that only the two samples of synthetic citral absorbed weakly.

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TABLE 1

Constants of Citral Samples Used

Source	B. p. (pressure in mm)	d_4^{20}	n_D^{20}	M. p. of semicarbazones
Technical	79° (2)	0.8900	1.4878	127—135°
From calcium chloride derivative of geraniol	82 (3)	0.8868	1.4878	—
From telomer of isoprene with prenyl chloride	90 (6)	0.8894	1.4862	137—142
From telomer of isoprene with dimethylvinylchloromethane	85 (4)	0.8893	1.4865	143
Geranial [7]	92—93 (2.6) *	0.8888	1.4852	164
Neral [7]	91—92 (2.6)	0.8869	1.4823	171

TABLE 2

Infrared Spectra of Various Citral Samples

Technical	From geraniol	From 1,2-hydrochloride of isoprene	From 1,4-hydrochloride of isoprene	Citral "a" [7]	Citral "b" [7]
733 о. сл	733 о. сл	743 ср	743 ср	—	—
817 ср	817 ср	817 ср	817 ср	820 ср	—
838 с	838 с	841 ср	841 ср	843 ср	843 с
862 сл	862 сл	864 сл	864 сл	866 ср	
889 о. сл	889 о. сл	889 сл	889 сл	892 сл	—
—	—	—	—	920 сл	—
984 с	984 с	984 с	984 с	985 ср	986 ср
1043 с	1043 с	1043 с	1043 с	1033 ср	1039 ср
				1045 сл	
				1105 сл	1098 сл
1118 о. с	1118 о. с	1118 о. с	1118 о. с	1121 с	1121 с
1154 с	1154 с	1154 ср	1154 с	1153 сл	1154 с
1190 о. с	1190 о. с	1190 о. с	1190 о. с	1189 с	1186 с
					1192 с
		1252 сл	1252 сл	—	—
1294 о. сл	1297 о. сл	1302 сл	1307 сл	1310 сл	1312 сл
1322 сл	1325 сл	1332 сл		1337 сл	1347 сл
1382 о. с	1382 о. с	1382 о. с	1382 о. с	1396 с	1394 с
		1402 о. с	1402 о. с		
1448 о. с	1448 о. с	1448 о. с	1448 о. с	1459 с	1456 с
1635 о. с	1635 о. с	1635 о. с	1635 о. с	1627 ср	1626 ср
1678 о. с	1678 о. с	1682 о. с	1684 о. с	1668 с	1664 с
2729 ср	2729 ср	2729 ср	2729 ср	⎫	
2767 ср	2767 ср	2767 ср	2767 ср	⎪	
2858 о. с	2858 о. с	2858 о. с	2858 о. с	Not plotted further	
2917 о. с	2917 о. с	2917 о. с	2917 о. с	⎪	
2966 о. с	2966 о. с	2966 о. с	2966 о. с	⎭	

[о. сл. = very weak, ср. = medium, с. = strong, сл = weak, о. с. = very strong]

Thus, it was established that the synthetic citral contained a terpineol form (or an impurity with the $CH_2=$ grouping). The presence of terpineol α-form is characteristic of synthetic products, especially if, as in our case, reagents of an acid character are used in their preparation [9].

EXPERIMENTAL

We obtained normal citral from a synthetic perfume factory. In addition, we prepared citral by oxidation of geraniol, obtained from linalool of coriander oil and purified through the compound with $CaCl_2$. The sample of geraniol used had the constants: b.p. 110° (10 mm), d_4^{20} 0.8813, n_D^{20} 1.4760.

TABLE 3

Raman Spectra of Various Citral Samples

Technical	From 1,2-hydrochloride of isoprene	From 1,4-hydrochloride of isoprene	Literature date [11]
988 (4)	998 (5)		
1005 (3)	—		1009 (6)
1039 (2)	1041 (3)		1041 (4)
—	—		1071 (1)
1119 (3)	1115 (5)	1121 (4)	1120 (4)
1152 (7)	1154 (3)	1156 (3)	1154 (10)
1190 (1)	1189 (8)	1188 (7)	1181 (10)
—	1222 (1)	1240 (0)	—
1279 (5)	1276 (1)	1278 (1)	1283 (2)
1329 (7)	1323 (7)	1329 (6)	1334 (5)
	1343 (?)	—	
1379 (7)	1377 (6)	1384 (6)	1382 (12)
1397 (7)	1403 (7)	1403 (6)	1400 (12)
—			1414 (12)
1445 (6)	1444 (5)	1447 (6)	1460 (12)
1628 (10)	1630 (10)	1631 (10)	1631 (15)
1670 (10)	1669 (10)	1670 (10)	1674 (18)
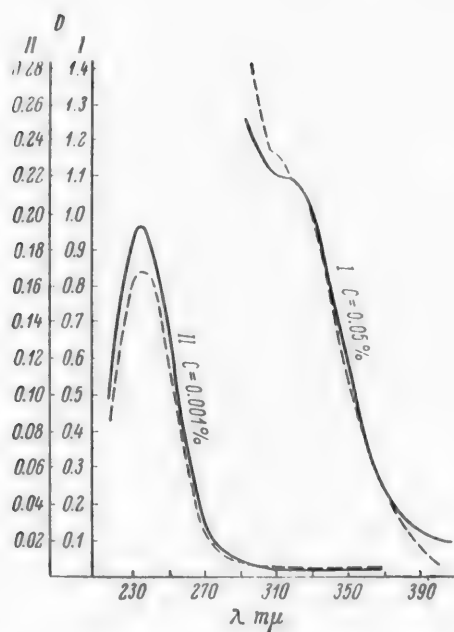
Fig. 2. Ultraviolet spectra of synthetic (solid line) and normal (broken line) citrals.

The synthetic citral was prepared by the Sommelet method from a fraction of terpene chlorides, obtained by telomerization of isoprene with its hydrochlorides [4, 10]. The constants of all the citral samples examined are given below (Table 1).

The infrared spectra were plotted on an IKS-12 spectrophotometer in the region $2.5-5\mu$ with an LiF prism and then with an NaCl prism. The overtones in the region of 1.6μ were plotted using a glass prism. The data obtained in are presented in Table 2 and Fig. 1.

The Raman spectra were plotted on an ISP-53 spectrograph, using a saturated $NaNO_2$ solution and a solution of iodine in CCl_4 as filters. The spectra were excited with the 4358 A mercury line. The data obtained are presented in Table 3.

The ultraviolet spectra were plotted on an SF-4 spectrophotometer in an ethanol solution in the region of $230-290$ mμ at a concentration of 0.001% and then at a contentration of 0.05%. The data obtained are presented in Table 4 and Fig. 2.

In an attempt to separate the semicarbazones of synthetic citral by chromatography on aluminum oxide, we isolated only the semicarbazone of geranial with m. p. 163.5° in a pure form.

The author would like to thank the All-Union Scientific Research Institute of Synthetic and Natural Aromatic Principles for help in carrying out this work.

TABLE 4

Maxima in the Ultraviolet Spectra of Various Citral Samples

Source of citral	K-band		R-band	
	λ_{max}	ϵ_{max}	λ_{max}	ϵ_{max}
From geraniol	238	12790	315	71
Synthetic	235	14610	315	67
Literature data [12]	235	13500	324	65

SUMMARY

1. An investigation was made of the infrared, Raman and ultraviolet spectra of synthetic critical, obtained from the telomers of isoprene with its hydrochlorides by the Sommelet reaction.

2. It was established that the samples of citral obtained from the two isomeric hydrochlorides of isoprene were practically identical.

3. It was shown that synthetic citral differed somewhat from the natural and technical materials and that this difference was apparently connected with a different content of the geometrical isomers (geranial and neral) and the presence of an impurity.

4. It was established that synthetic citral contained a small amount of an α-form.

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THE CHEMISTRY OF VINYLACETYLENE

XL THE MECHANISM AND DIRECTION OF THE HYDRATION OF ETHERS OF VINYLETHYNYLCARBINOLS

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It was previously shown that on hydrating acetates of vinylethynylcarbinols in acetic acid in the presence of mercury salts, the addition of water to the acetylene bond proceeded in only one direction with the formation of unsaturated α-acetoxyketones [1].

It seemed interesting to study the hydration of ethers of vinylethynylcarbinols to determine the direction by which the elements of water are added to the triple bond. It was found that the ethers, in contrast to the esters of vinylethynylcarbinols were smoothly converted to β-keto derivatives in alcohol solutions in the presence of mercuric sulfate. Thus, for example, when the methyl ethers of vinylethynylcarbinol (I), methylvinylethynylcarbinol (II) and dimethylvinylethynylcarbinol (III) were heated (50-65°) with 90% methanol in the presence of mercuric sulfate, the final products formed were the corresponding β-methoxy ketones (IV)-(VI).

(I) R = R' = H,
(II) R = H, R' = CH₃,
(III) R = R' = CH₃.

(IV) R = R' = H,
(V) R = H; R' = CH₃,
(VI) R = R' = CH₃.
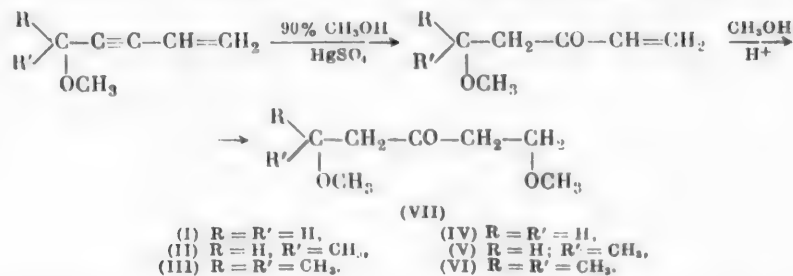
Thus, in the hydration of ethers of vinylethynylcarbinols, in contrast to the esters, water was added to the triple bond in the direction which gave β-methoxyvinyl ketones (VII) and under the reaction conditions the latter added methanol and were converted to β,β'-dimethoxy ketones.

Together with the formation of the normal reaction product, the dimethoxy ketone (VI), hydration of the methyl ether (III) let largely to the formation of the unsaturated β-methoxy ketone (VIII). This is apparently explained by the instability of the tertiary β-methoxy-β'-vinyl ketone (VII, R = R' = CH₃), which is cleaved at the moment of formation, under the hydration conditions, and, through the divinyl ketone (IX), again adds methanol to form the β-methoxy ketone (VIII).

As would be expected, the hydration of the tertiary methyl ether (III) in ethanol solution in the presence of mercuric sulfate gave the β-ethoxy ketone (X) and moreover, it was possible to isolate the intermediate product — the divinyl ketone (IX).

(VIII)

(X)

$$CH_3 \diagdown C=CH-CO-CH=CH_2$$
$$CH_3 \diagup$$
$$(IX)$$

$$CH_3 \diagdown C-C\equiv C-CH=CH_2$$
$$CH_3 \diagup \underset{OC_2H_5}{|}$$
$$(XI)$$
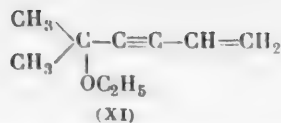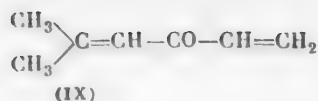
A similar result was obtained in the hydration of the ethyl ether of dimethylvinylethynylcarbinol (XI) in ethanol solution in the presence of mercuric sulfate.

It is interesting to note that when the vinyl group in the methyl ethers of vinylethynylcarbinols is replaced by a methyl group, the order of water addition remains the same and the hydration rate increases strongly. Thus, the hydration of the methyl ether of methylethynylcarbinol (XII) in 90% methanol in the presence of mercuric sulfate proceeds even at room temperature to give a high yield of the β-methoxy ketone (XIII).

$$\underset{OCH_3}{\overset{}{CH_2-C\equiv C-CH_3}} \rightarrow \underset{OCH_3}{\overset{}{CH_2-CH_2-CO-CH_3}}$$
$$(XII) \qquad (XIII)$$

Hydrating the acetate of methylethynylcarbinol (XIV) in 90% acetic acid in the presence of mercuric sulfate or acetate yielded the β-acetoxy ketone (XV), i.e., as with ether (XII), the addition of water proceeds in the direction forming the β-keto derivative.

$$\underset{OCOCH_3}{\overset{}{CH_2-C\equiv C-CH_3}} \rightarrow \underset{OCOCH_3}{\overset{}{CH_2-CH_2-CO-CH_3}}$$
$$(XIV) \qquad (XV)$$
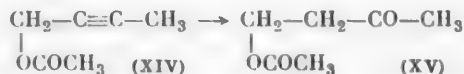
However, under similar hydration conditions, the acetate of the vinylethynylcarbinol (XVI) forms the α-keto derivative (XVII), which is isomerized under the reaction conditions to the acetate of crotonylcarbinol (XVIII).

$$\underset{OCOCH_3}{\overset{}{CH_2-C\equiv C-CH=CH_2}} \rightarrow \underset{OCOCH_3}{\overset{}{CH_2-CO-CH_2-CH=CH_2}} \rightarrow \underset{OCOCH_3}{\overset{}{CH_2-CO-CH=CH-CH_3}}$$
$$(XVI) \qquad\qquad (XVII) \qquad\qquad (XVIII)$$
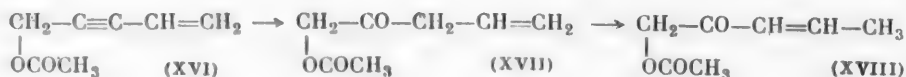
Previously, I. N. Nazarov and one of us proposed that the hydration mechanism of acetylene γ-glycols consisted of the addition of mercuric sulfate to the triple bond with the formation of a six-membered organomercury adduct, which was hydrolyzed to a carbonyl compound under the reaction conditions [2].
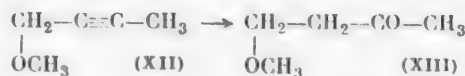
The order of the electrophilic addition of mercuric sulfate is apparently determined by the displacement of the π-electron pair toward one of the carbon atoms, depending on the character of the substituents at the triple bond.
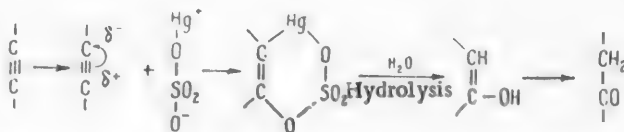
We should note that when sulfuric acid is introduced into the reaction mixture, the rate of hydration of ethers of both methylethynylcarbinol and vinylethynylcarbinols is increased considerably. As is known, in an acid medium, ethers are able to form oxonium compounds, which are apparently capable of increasing the polarity (displacing the π-electron pair) of the triple bond, on the one hand, and hindering the combination of the catalyst (mercuric sulfate) with the ether oxygen, on the other. Actually, the methyl ethers of vinylethynylcarbinols could not be hydrated in dioxane solution due to the great tendency of the latter to combine with acids and acid salts, forming oxonium compounds.

The triple bond in ether (XII) is polarized, not only due to the electron attraction of the oxonium ion, but also from the action of the electron donating methyl group and consequently, the two substituents promote polarization in one direction.

The polarizability of the triple bond in the ethers of vinylethynylcarbinol (I) – (III) is comparatively low due to the contrary effect of the electron-accepting vinyl group. Therefore, ether (XII), which has a more polarized triple bond than ether (I), is not only hydrated more readily, but in contrast to the former, adds methanol in the presence of mercuric sulfate to form trimethoxybutane (XIX).

$$CH_3 \underset{\overset{|}{H}}{\overset{\cdot \cdot}{O}}-CH_2 \leftarrow \overset{\cdot}{C} \underset{\delta^-}{\overset{}{\equiv}} \underset{\delta^+}{C} \leftarrow CH_3 \qquad CH_3-\underset{\overset{|}{H}}{\overset{\cdot \cdot}{O}}-CH_2 \leftarrow \overset{\cdot}{C} \underset{\delta^-}{\equiv} \underset{\delta^+}{C}-CH=CH_2 \qquad CH_3OCH_2CH_2\underset{\overset{|}{OCH_3}}{\overset{\overset{OCH_3}{|}}{C}}-CH_3$$

$$\text{(XII)} \qquad\qquad\qquad \text{(I)} \qquad\qquad\qquad \text{(XIX)}$$
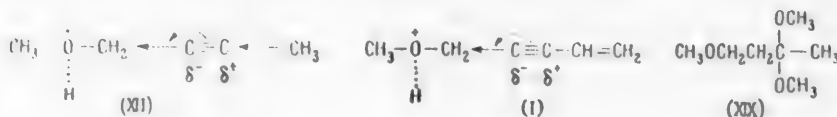
The direction of hydration of the triple bond in esters of methylethynylcarbinol (XIV) and vinylethynylcarbinol (XVI), which are unable to form oxonium salts, are only determined by the oppositely acting methyl and vinyl groups.

$$CH_3COOCH_2\overset{\frown}{C} \underset{\delta^-}{\equiv} \underset{\delta^+}{C} \leftarrow CH_3 \qquad\qquad CH_3COO-CH_2-C \underset{\delta^+}{\equiv} \underset{\delta^-}{\overset{\frown}{C}}-CH \overset{\frown}{=} CH_2$$

$$\text{(XIV)} \qquad\qquad\qquad\qquad \text{(XVI)}$$
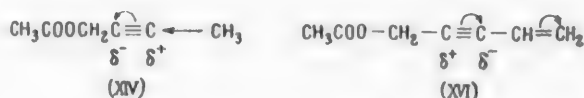
The structure of the hydration products was proved by the identification of crystalline derivatives (2,4-dinitrophenylhydrazones and semicarbazones) and also by hydrolysis, aminolysis, acetolysis, cleavage, etc.

EXPERIMENTAL

The methyl ether of methylethynylcarbinol (XII) was prepared by a known method [3] and had b. p. 95-96.5° (680 mm), $n^{20}D$ 1.4224.

The acetate of methylethynylcarbinol (XIV) was prepared by acetylating methylethynylcarbinol with acetic anhydride in the presence of sulfuric acid; b. p. 150-152° (680 mm), $n^{20}D$ 1.439 [3].

The methyl ether of vinylethynylcarbinol (I) was prepared according to a previous report [4]; b. p. 37° (20 mm), $n^{20}D$ 1.4610.

The acetate of vinylethynylcarbinol (XVI) was prepared by acetylating vinylethynylcarbinol with acetic anhydride in the presence of sulfuric acid.

B. p. 71-75° (16-17 mm), $n^{20}D$ 1.4660, d^{20}_4 0.9955, MR 34.44. $C_7H_8O_2F_F$. Calculated 33.71.
Found %: C 67.70, 67.72, H 6.49, 6.65. $C_7H_8O_2$. Calculated %: C 67.74; H 6.45.

The methyl ether of methylvinylethynylcarbinol (II) was prepared according to I. N. Nazarov's method [5] by boiling methylvinylethynylcarbinol with a 3-fold excess of methanol in the presence of sulfuric acid.

B. p. 33.5-34° (18 mm), $n^{20}D$ 1.4505, d^{20}_4 0.8145, MR 36.37. $C_7H_{10}OF_F$. Calculated 37.00.
Found %: C 76.17, 76.04; H 9.20, 9.25. $C_7H_{10}O$. Calculated %: C 76.36; H 9.09.

The methyl ether of dimethylvinylethynylcarbinol (III) was prepared according to report of I. N. Nazarov [5]. B. p. 33-34° (11 mm), $n^{20}D$ 1.4530.

The ethyl ether of dimethylvinylethynylcarbinol was also prepared according to a report of I. N. Nazarov [5]. B. p. 46-47° (16 mm), $n^{20}D$ 1.4545.

Hydration of the methyl ether of vinylethynylcarbinol (I). a) Into a three-necked flask fitted with a reflux condenser, a mechanical stirrer and a thermometer was placed 30 g of the ether, 150 g of 90% methanol and 3 g of mercuric sulfate (introduced in portions). The mixture was heated on a water bath at 60-65° for 30 hours. The methanol was distilled off under reduced pressure and the residue treated with an aqueous solution of potassium carbonate, extracted with ether and dried with magnesium sulfate. We obtained 20.5 g (45%) of β,β'-dimethoxydiethyl ketone (IV). The b.p. was 78-82° (8-9 mm), $n^{20}D$ 1.4250 [6].

b) The same amounts of starting materials and catalyst were taken for the reaction with the addition of 0.7 ml of concentrated sulfuric acid. The reaction mixture was stirred at 40-65° for 14 hours. Working up the residue as above yielded 28.8 g (63%) of β,β'-dimethoxydiethyl ketone (IV) with b.p. 80° (9 mm), $n^{20}D$ 1.4245 [6]

When 5 g of the dimethoxy ketone obtained (IV) was aminolyzed with 20 g of 33% dimethylamine in a sealed ampule at 60-70° for 4 hours and the product worked up normally, we obtained 2.4 g of β,β'dimethyl-aminodiethyl ketone with b. p. 85-86° (6 mm), $n^{20}D$ 1.4480, whose oxalate melted at 155° (from ethanol)[7].

Hydrolysis of 8 g of the dimethoxy ketone (IV) with 30 g of 25% sulfuric acid and 0.5 g of mercuric sulfate at 75-80° for 8 hours gave 3 g of tetrahydro-γ-pyrone with b.p. 69-71° (24 mm), $n^{20}D$ 1.4545. The semicarbazone melted at 174-175° (from water) and did not depress the melting point of authentic sample [6].

Hydration of the methyl ether of methylvinylethynylcarbinol (II). A mixture of 10 g of ether (II), 30 g of 90% methanol and 1 g of mercuric sulfate was stirred at 60-65° for 6 hours. Working up in the usual way yielded 8 g of β-methoxyethyl β'-methoxypropyl ketone (V) with b.p. 83-84° (9 mm), 61° (3 mm), $n^{20}D$ 1.4260 [8]. When 5.5 g of the dimethoxy ketone (V) obtained was stirred with 20 g of 15% sulfuric acid at 70-75° for 4 hours and the hydrolysis product worked up tin the usual way, we obtained 2.5 g of 1-methyltetra-hydro-1-pyrone with b.p. 60-61 (14 mm), $n^{20}D$ 1.4430. The semicarbazone melted at 169-171° (from water) and did not depress the melting point of an authentic sample [8].

Hydration of the methyl ether of dimethylvinylethynylcarbinol (III). a) A mixture of 15 g of freshly distilled ether, 45 g of 90% methanol and 1 g of mercuric sulfate was heated at 60-65° and stirred for 6 hours. Working up as described above yielded 14 g of 1-methoxy-5-methyl-4-hexenone-3 (VIII) with b.p. 75-76° (8 mm), $n^{20}D$ 1.4547 [9]. The 2,4-dinitrophenylhydrazone of the methoxy ketone (VIII) melted at 107-108° (from alcohol) and did not depress the melting point of an authentic sample [10].

b) A mixture of 10 g of ether (III), 30 g of 90% methanol, containing 0.5 ml of concentrated sulfuric acid and 1 g of mercuric sulfate was stirred at 35-40° for 2 hours. The product was isolated as in the previous experiment. We obtained 8.4 g of the monomethoxy ketone (VIII) with b. p. 80-82° (10 mm), $n^{20}D$ 1.4555, the 2,4-dinitrophenylhydrazone of which melted at 106-108° [10], and 0.6 g of 1,5-dimethoxy-5-methylhexanone-3 (VI) with b.p. 90-93° (10 mm), $n^{20}D$ 1.4390 [11].

When the ether was hydrated in 90% dioxane in the presence of mercuric sulfate at 60-70°, the original ether (III) taken was recovered unchanged.

Hydrolysis of 10 g of the mixture of the monomethoxy ketone (VIII) and the dimethoxyketone (VI) with 30 g of 15% sulfuric acid yielded 4 g of 2,2-dimethyltetrahydro-4-pyrone with b.p. 50-51° (5 mm), $n^{20}D$ 1.4465. The semicarbazone melted at 165° and did not depress the melting point of an authentic sample [12].

The acetolysis of 20 g of the methoxy ketone (VIII) with 37 g of acetic anhydride, 40 g of acetic acid and 2 g of anhydrous sodium acetate yielded 9 g of 1-acetoxy-5-methyl-4-hexenone-3 with b. p. 92-93° (5 mm), $n^{20}D$ 1.4600. The semicarbazone melted at 133-134° and did not depress the melting point of an authentic sample [13].

Hydration of the methyl ether of dimethylvinylethynylcarbinol (III) in 90% ethanol. A mixture of 15 g of ether, 50 g of 90% ethyl alcohol and 1 g of mercuric sulfate was stirred at 65-75° for 8 hours. Working up in the usual way yielded 2 g of β,β'dimethyldivinyl ketone (IX) with b.p. 43-45° (10 mm), $n^{20}D$ 1.4825 and 10.3 g of 1-ethoxy-5-methyl-4-hexenone-3 (X) with b.p. 83-84° (10 mm), $n^{20}D$ 1.4540, whose semicarbazone melted at 126-127° and did not depress the melting point of an authentic sample [9].

Hydration of the ethyl ether of dimethylvinylethynylcarbinol (XI). A mixture of 20 g of the ethyl ether, 50 g of 90% ethanol and 3 g of mercuric sulfate was stirred at 60-70° for 8 hours. The product was worked up as described above. We obtained 13.5 g of 1-ethoxy-5-methyl-4-hexenone-3 (X) with b.p. 84-86° (10 mm), $n^{20}D$ 1.4565. The semicarbazone melted at 125-127° and did not depress the melting point of an authentic sample [9].

Hydration of the methyl ether of methylethynylcarbinol (XII). a) A mixture of 15 g of the ether, 45 g of 90% methanol and 1 g of mercuric sulfate was stirred at 40-60° for 6 hours. The substance was isolated as described above. We obtained 11 g of methyl β-methoxyethyl ketone (XIII) with b.p. 34-36° (11 mm), 134-136° (680 mm), $n^{20}D$ 1.4050. The 2,4-dinitrophenylhydrazone melted at 84-86° and did not depress the melting point of an authentic sample [14].

b) When 15 ml of 90% methanol, containing 0.5 ml of concentrated sulfuric acid, was added to a mixture of 5 g of ether (XII) and 1 g of mercuric sulfate, heat was evolved and the temperature rose to the boiling point

of the methanol (65°). The reaction mixture was stirred at 30-35° for 2 hours. Working up in the usual way 80 yielded 4 g of methyl β-methoxyethyl ketone (XII) with b. p. 134-136 (680 mm), $n^{20}D$ 1.4050 [14].

When 5 g of the methoxy ketone (XIII) was distilled in the presence of 0.005 g of p-toluenesulfonic acid, we obtained 2.4 g of methyl vinyl ketone with b.p. 78-80° (680 mm), $n^{20}D$ 1.4460. The semicarbazone melted at 140° and did not depress the melting point of an authentic sample [15].

Aminolysis of 7 g of the methoxy ketone (XIII) with 15 ml of 33% dimethylamine yielded 4.8 g of methyl β-dimethylaminoethyl ketone with b.p. 65-67° (22 mm), $n^{20}D$ 1.4320. The picrate melted at 107° (from water) and did not depress the melting point of an authentic sample [16].

Addition of methanol of the methyl ether of methylethynylcarbinol (XII). When 7 g of the methyl ether, 20 g of anhydrous methanol and 1 g of mercuric sulfate were mixed, the temperature of the reaction mixture rose to 45°. The reaction mixture was then heated on a water bath at 30-35° for 2 hours. The reaction product was neutralized with a methanol solution of sodium methylate, the methanol removed under reduced pressure and the residue extracted with ether, washed with water and dried over magnesium sulfate. We obtained 7.5 g (61%) of 1,3,3-trimethoxybutane (XIX) with b.p. 53-54° (15 mm), 150-151° (671 mm), $n^{20}D$ 1.4100 [17].

When 5 g of trimethoxybutane was hydrolyzed with 5 ml of water, containing 2 drops of hydrochloric acid, we obtained 2.2 g of methyl β-methoxyethyl ketone with b.p. 134-136° (680 mm), $n^{20}D$ 1.4050. The 2,4-dinitrophenylhydrazone melted at 85-86° and did not depress the melting point of an authentic sample [14].

Hydration of the acetate of methylethynylcarbinol (XIV). a) A mixture of 5 g of the butynol acetate, 15 g of 90% acetic acid and 1 g of mercuric sulfate was stirred at 40-45° for 6 hours. The acetic acid was removed under water-pump vacuum at 30-40° and the residue treated with sodium bicarbonate, extracted with ether and dried with magnesium sulfate. We obtained 2 g of the original acetate (XIV) with b.p. 150-152° (680 mm), $n^{20}D$ 1.4350 and 1.6 g of methyl-β-acetoxyethyl ketone (XV) with b.p. 80-82°(10 mm), 176-178° (680 mm), $n^{20}D$ 1.4230, whose semicarbazone melted at 135-136° and did not depress the melting point of an authentic sample [13].

b) A mixture of 10 g of the butynol acetate, 30 g of 90% acetic acid and 1 g of mercuric acetate was boiled under reflux for 6 hours. The reaction product was distilled twice in vacuum. We obtained 8.5 g (73%) of methyl β-acetoxyethyl ketone (XV) with b.p. 79-83° (10-11 mm), $n^{20}D$ 1.4235. The semicarbazone melted at 135-136° and did not depress the melting point of an authentic sample [13].

5 g of the β-acetoxy ketone (XV) was heated in the presence of 1 g of anhydrous sodium acetate at 120-150°. When the acetic acid had been neutralized with potassium carbonate, the cleavage product was extracted with ether and distilled at atmospheric pressure. We obtained 2 g of methyl vinyl ketone with b.p. 78-80° (680 mm), whose semicarbazone melted at 140-141° and did not depress the melting point of an authentic sample [15].

Hydration of the acetate of vinylethynylcarbinol (XVI). 14 g of acetate in 15 ml of acetic acid was added dropwise over a period of 1.5 hours with stirring to a mixture of 80 g of 90% acetic acid 0.5 g of mercuric sulfate, heated to 40°. The reaction mixture was then stirred at 40-50° for 4 hours. The acetic acid was removed in vacuum and the residue treated with aqueous potassium carbonate solution, extracted with ether and dried with magnesium sulfate. We obtained 7.5 g of the acetate of crotonoylcarbinol (XVIII).

B. p. 64-65° (2 mm), 60-61° (1.5 mm), $n^{20}D$ 1.4520, d^{20}_4 1.05774, MR 36.02. $C_7H_{10}O_3F$. Calculated 35.72.
Found %: 58.77, 58.87; H 7.16, 7.01. $C_7H_{10}O_3$. Calculated %: C 59.15; H 7.04.

The 2,4-dinitrophenylhydrazone melted at 145-147° (from ethyl acetate).

Found %: N 17.19, 17.43. $C_{13}H_{14}O_6N_4$. Calculated %: N 17.37.

When the acetoxy ketone (XVIII) obtained was heated in the presence of sodium acetate in vacuum (100 mm) at 120-180°, the product was recovered unchanged, indicating that it was an α-keto derivative [1].

3.5 g of substance (XVI) was hydrogenated in 10 ml of alcohol over a Pt-catalyst. The theoretical amount of hydrogen, required for one double bond, was absorbed. We obtain 3 g of the acetate of butyryl-carbinol as a mobile liquid with a fruity smell.

B. p. 94-96° (16 mm), $n^{20}D$ 1.4210, d^{20}_4 1.0170, MR 35.91; calc. 36.19.
Found %: C 58.06, 58.25; H 8.64, 8.60. $C_7H_{12}O_3$. Calculated %: C 58.33, H 8.33

SUMMARY

1. It was shown that in the hydration of ethers of vinylethynylcarbinols in alcohol solutions in the presence of mercuric sulfate, unlike the case of esters, the addition of water to the triple bond proceeds in the direction yielding β-keto derivatives.

2. It was established that both the acetate and the methyl ether of methylethynylcarbinol are hydrated in the presence of mercury salts in one direction to form the β-keto derivative.

3. It was shown that like the acetates of other secondary and tertiary vinylethynylcarbinols, the acetate of vinylethynylcarbinol is hydrated in the direction giving the α-keto derivative.

4. An attempt was made to explain the direction of hydration of ethers of vinylethynylcarbinols and methylethynylcarbinols in relation to the order of electrophilic addition of mercuric sulfate (the elements of water) to the triple bond.

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PREPARATION OF AMIDES OF β-CARBOXYETHYL ETHERS OF DIMETHYL-β-BROMOETHYNYLCARBINOL AND 1-(β-BROMOETHYNYL)-CYCLOHEXANOL-1

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In continuing our investigations on the cyanoethylation of acetylene alcohols [1, 2] and further conversions of the β-cyanoethyl ethers obtained [3, 4], we carried out the addition of some bromine substituted acetylene alcohols to acrylonitrile and a series of conversions of the β-cyanoethyl ethers thus obtained.

By the action of KOBr on acetylene alcohols [5], we obtained dimethyl-β-bromoethynylcarbinol (I), 1-(β-bromoethynyl)-cyclohexanol-1 (II) and methylphenyl-β-bromoethynylcarbinol (III).
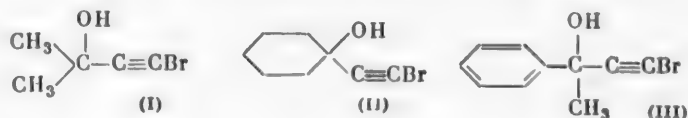
These alcohols readily added to acrylonitrile in the presence of a 40% aqueous solution of potassium hydroxide with the formation of the corresponding β-cyanoethyl ethers (IV).
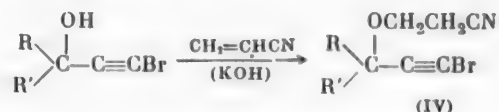
The same bromine substituted β-cyanoethyl ethers (IV) were obtained by bromination of the β-cyanoethyl ethers (V-VII).
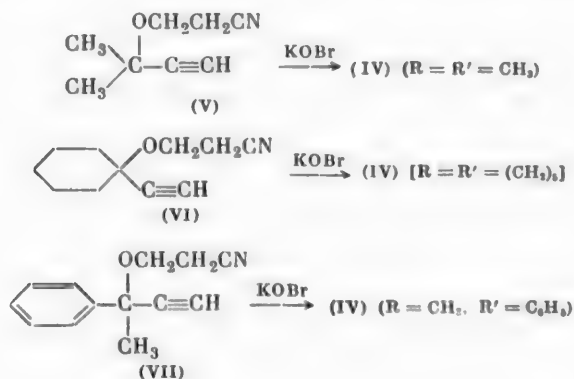
Treatment of the β-cyanoethyl ethers (IV) (R = R' = CH₃) and [R = R' = (CH₂)₅] with methyl alcohol, saturated with dry hydrogen chloride [3], followed by hydrolysis converted them into the corresponding β-carbomethoxyethyl ethers (VIII).

The β-cyanoethyl ether (IV) (R = CH₃, R' = C₆H₅) could not undergo a similar conversion due to its extreme sensitivity to strong acids.
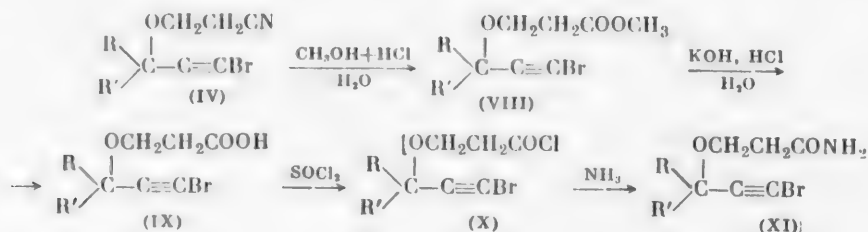
The ethers (VIII) were smoothly hydrolyzed into β-carboxyethyl ethers (IX) by an aqueous alcohol solution of sodium hydroxide at room temperature [4].

When treated with thionyl chloride, the acids (IX) readily gave the acid anhydrides (X), which reacted quantitatively with gaseous ammonia to give the amides of the β-carboxyethyl ethers of the corresponding acetylene alcohols [4] (XI).

It is known that many compounds containing an amide group or a halogen atom in the molecule [6], like many acetylene alcohols [7], have a soporific effect. At the present time pharmacological tests are being performed on the amides obtained (XI).

<center>EXPERIMENTAL</center>

Bromination of Acetylene Alcohols

The reactions were performed in a three-necked flask fitted with a mechanical stirrer, a thermometer and a dropping funnel.

Dimethyl-β-bromoethynylcarbinol (I). With vigorous stirring, a cold solution prepared by adding 16 ml of bromine to 110 g of potassium hydroxide in 450 ml of water at 0° was added over a period of 45 minutes to 25.2 g of dimethylethynylcarbinol; the mixture was kept at 5-8° by external cooling, stirred for 45 minutes at 5-20°, saturated with sodium chloride and extracted with ether and the ether extract dried over sodium sulfate and distilled. We obtained 47.4 g (97%) of dimethyl-β-bromoethynylcarbinol (I) with b.p. 58-60° (10 mm) [5].

1-(β-Bromoethynyl)-cyclohexanol-1 (II). With vigorous stirring, a solution of KOBr (from 11 ml of bromine and 80 g of potassium hydroxide in 300 ml of water) was added over a period of 30 minutes to a mixture of 24.8 g of 1-ethynylcyclohexanol-1 and 25 ml of petroleum ether at 8-10° and the reaction mixture was stirred at room temperature for 8 hours, left overnight and treated as described above. We obtained 39.4 g (97%) of 1-(β-bromoethynyl)-cyclohexanol-1 (II) with b.p. 100-102° (7 mm) and m.p. 55-56° [5].

Methylphenyl-β-bromoethynylcarbinol (III). With vigorous stirring, a solution prepared from 11 ml of bromine and 80 g of potassium hydroxide in 300 ml of water was added over 30 minutes to a mixture of 29.2 g of methylphenylethynylcarbinol and 30 ml of petroleum ether at 8-10° and the reaction mixture was stirred at room temperature for 6 hours and treated as usual. We obtained 43.6 g (97%) of methylphenyl-β-bromoethynylcarbinol (III) with b.p. 106-107° (2 mm) and m.p. 52-54° (from benzene).

Found %: C 53.70; 53.62; H 3.96, 3.85; Br 35.46, 35.61. C₁₀H₉OBr. Calculated %: C 53.33; H 4.00; Br 35.55.

Cyanoethylation of Brominated Acetylene Alcohols

β-Cyanoethyl ether of dimethyl-β-bromoethynylcarbinol (IV, R = R' = CH₃). Into a three-necked flask, fitted with a mechanical stirrer, a thermometer and a dropping funnel, was placed 29 g of dimethyl-β-bromoethynylcarbinol and 2.5 g of a 40% aqueous solution of sodium hydroxide. Over a period of 20 minutes, 10 g of acrylonitrile was added with vigorous stirring. The temperature of the mixture gradually increased to 30°

and then fell to 20° over 2 hours. The reaction mixture was stirred at room temperature for 4 hours, left overnight and neutralized with hydrochloric acid (1 : 1). The mixture was diluted with ether, the aqueous layer separated and the ether solution dried over magnesium sulfate and fractionated in vacuum. The unreacted starting alcohol (10.7 g) distilled over first at 51-54° (10 mm), followed by 23 g (91%) of the β-cyanoethyl ether of dimethyl-β-bromoethynylcarbinol (IV, R = R' = CH₃).

B. p. 107-109° (6 mm), 112-114° (7 mm), $n^{20}D$ 1.4796, d^{20}_4 1.3277, MR_D 46.18; calc. 46.31.
Found %: N 6.57, 6.64. $C_8H_{10}ONBr$. Calculated %: N 6.48.

β-Cyanoethyl ether of 1-(β-bromoethynyl)-cyclohexanol-1 [IV, RR' = (CH₂)₅]. 6 g of acrylonitrile was added over 15 minutes to a vigorously stirred mixture of 20.3 g of 1-(β-bromoethynyl)-cyclohexanol-1, 20 ml of dioxane and 2 g of aqueous 40% potassium hydroxide solution; a slight increase in temperature was observed. The reaction mixture was stirred for 4 hours, left overnight, stirred for 7 hours, left for two days and stirred for a further 9 hours. The alkali was neutralized with hydrochloric acid (1 : 1), 200 ml of ether added, the water separated and the ether solution dried over magnesium sulfate and distilled. We obtained 17.5 g (83%, calculated on the reacted alcohol) of the β-cyanoethyl ether of 1-(β-bromoethynyl)-cyclohexanol-1.

B. p. 148-150° (6 mm), 137-139° (3 mm), $n^{20}D$ 1.4944, d^{20}_4 1.2812, MR_D 58.21; calc. 57.86.
Found %: N 5.43, 5.44. $C_{11}H_{14}ONBr$. Calculated %: N 5.47.

In addition, 3.3 g of the original carbinol was recovered.

β-Cyanoethyl ether of methylphenyl-β-bromoethynylcarbinol (IV, R = CH₃ and R' = C₆H₅). 12 g of acrylonitrile was added over a period of 20 minutes to a vigorously stirred mixture of 43.5 g of methylphenyl-β-bromoethynylcarbinol, 15 ml of dioxane and 5 g of 40% aqueous potassium hydroxide; a slight rise in temperature was observed. The reaction mixture was stirred for 6 hours, left overnight, neutralized with hydrochloric acid (1 : 1) and treated as described above. We obtained 29.5 g (99%, calculated on the reacted alcohol) of the β-cyanoethyl ether of methylphenyl-β-bromoethynylcarbinol.

B. p. 147-151° (3 mm), $n^{20}D$ 1.5408, d^{20}_4 1.3139, MR_D 66.46; calc. 65.79.
Found %: N 5.14, 5.28. $C_{13}H_{12}ONBr$. Calculated %: N 5.04.

Bromination of β-Cyanoethyl Ethers of Acetylene Alchols

β-Cyanoethyl ether of dimethyl-β-bromoethynylcarbinol (IV, R = R' = CH₃). With vigorous stirring, a solution of KOBr (from 80 g of potassium hydroxide and 11 ml of bromine in 300 ml of water) was added over a period of 30 minutes with vigorous stirring to 27.4 g of the β-cyanoethyl ether of dimethylethynylcarbinol (V) (b. p. 100° at 22 mm). The temperature of the mixture was kept at 8-10° by external cooling. The reaction mixture was left to heat up to room temperature, while stirred, and then stirred for a further 2 hours. The product was extracted with ether and the ether solution dried with magnesium sulfate and distilled. We obtained 42.7 g (97%) of the β-cyanoethyl ether of dimethyl-β-bromoethynylcarbinol with b. p. 110-111° (6.5 mm), $n^{20}D$ 1.4789.

β-Cyanoethyl ether of 1-(β-bromoethynyl)-cyclohexanol-1 [IV, RR' = (CH₂)₅]. A solution of KOBr (from 40 g of potassium hydroxide and 5.5 ml of bromine in 150 ml of water) was added with vigorous stirring to 17.7 g of the β-cyanoethyl ether of 1-ethynylcyclohexanol-1 (VI) (b. p. 92-95° at 3 mm) [2], while the temperature of the mixture was kept below 10°, then the mixture was stirred for 8 hours at room temperature and left overnight. The product was extracted with ether, dried with magnesium sulfate and distilled. We obtained 16.6 g (92%, calculated on the original β-cyanoethyl ether, when reacted) of the β-cyanoethyl ether of 1-(β-bromoethynyl)-cyclohexanol-1 with b.p 148-151° (6 mm), $n^{20}D$ 1.4948.

5.3 g of the original β-cyanoethyl ether was recovered from the reaction.

β-Cyanoethyl ether of methylphenyl-β-bromoethynylcarbinol (IV, R = CH₃ and R' = C₆H₅). Under conditions similar to those of the previous experiment, 19.9 g of the β-cyanoethyl ether of methylphenylethynylcarbinol (VII) (b.p. 115-118° at 3.5 mm) [2], 40 g of potassium hydroxide, 5.5 ml of bromine and 150 ml of water yielded 13.6 g (89%, calculated on the original β-cyanoethyl ether which reacted) of the β-cyanoethyl ether of methylphenyl-β-bromoethynylcarbinol with b.p. 132-134° (1 mm), $n^{20}D$ 1.5418; 9 g of the original β-cyanoethyl ether was recovered.

Alcoholysis of β-Cyanoethyl Ethers [IV, R = R'=CH₃ and RR' = (CH₂)₅]

β-Carbomethyoxyethyl ether of dimethyl-β-bromoethynylcarbinol (VIII, R = R' = CH₃). A solution of 43.2 g of the β-cyanoethyl ether of dimethyl-β-bromoethynylcarbinol in 240 ml of methyl alcohol, containing 46 g of dry hydrogen chloride, was kept at room temperature for 20 hours. The methanol was removed in vacuum at a water bath temperature of not more than 40°, the residue treated with 300 ml of water and the product extracted with ether. The ether solution was washed three times with a saturated aqueous solution of sodium bicarbonate and dried with magnesium sulfate. After distilling off the ether, we obtained 47.7 g (95%) of the β-carbomethoxyethyl ether of dimethyl-β-bromoethynylcarbinol with m.p. 45-46° (from petroleum ether.

Found %: C 43.64, 43.70; H 5.31, 5.32; Br 32.64, 32.60. $C_9H_{13}O_3Br$. Calculated %: C 43.37; H 5.22; Br 32.13.

β-Carbomethoxyethyl ether of 1-(β-bromoethynyl)-cyclohexanol-1 [VIII, RR' = (CH₂)₅]. From 36.5 g of the β-cyanoethyl ether of 1-(β-bromoethynyl)-cyclohexanol-1 and 190 ml of methyl alcohol, containing 36 g of dry hydrogen chloride we obtained 37.8 g (91%) of the β-carbomethoxyethyl ether of 1-(β-bromoethyn-yl)-cyclohexanol-1 as described above.

B.p. 145-146° (7 mm), n^{20}D 1.4970, d^{20}_4 1.3117, MR_D 64.18; Calc. 64.41.
Found %: C 50.09, 50.24; H 5.79, 5.84; Br 27.28, 27.46. $C_{12}H_{17}O_3Br$. Calculated %: C 49.83; H 5.88; Br 27.68.

Hydrolysis of β-Carbomethoxyethyl Ethers [VIII, R = R' = CH₃ and RR' = (CH₂)₅]

β-Carboxyethyl ether of dimethyl-β-bromothynylcarbinol (IX, R = R' = CH₃). 45 g of the β-carbometh-oxyethyl ether of dimethyl-β-bromoethynylcarbinol was added to a solution of 18 g of sodium hydroxide in 360 ml of methyl alcohol and 18 ml of water. The mixture was kept at room temperature for 2 hours. A stream of carbon dioxide was passed through the solution until the Na₂CO₃ was completely precipitated and the precipitate was filtered off and washed with methyl alcohol. The filtrate was evaporated to dryness in vacuum. After re-moval of the methanol, the residue and the precipitate from the filter were combined and treated with 250 ml of hydrochloric acid (1 : 1) and the product extracted with ether. After removal of the ether, we obtained 41.1 g (97%) of the β-carboxyethyl ether of dimethyl-β-bromoethynylcarbinol with m.p. 61-63° (from petroleum ether).

Found %: C 41.02, 41.21; H 4.77, 4.84; Br 34.38, 34.65. $C_8H_{11}O_3Br$. Calculated %: C 40.85; H 4.68; Br 34.04.

β-Carboxyethyl ether of 1-(β-bromoethynyl)-cyclohexanol-1 [IX, RR' = (CH₂)₅]. 30 g of the β-carbo-methoxyethyl ether of 1-(β-bromoethynyl)-cyclohexanol-1 and 12 g of sodium hydroxide in 250 ml of methyl alcohol and 12 ml of water similarly yielded 28.3 g (99%) of the β-carboxyethyl ether of 1-(β-bromoethynyl)-cyclohexanol-1 with m.p. 101-102° (from petroleum ether).

Found %: C 48.09, 48.07; H 5.46, 5.40; Br 28.78, 28.83. $C_{11}H_{15}O_3Br$. Calculated %: C 48.00; H 5.45; Br 29.09.

Reaction of β-Carboxyethyl Ethers [IX, R = R' = CH₃ and RR' =(CH₂)₅] with Thionyl Chloride.

A mixture of 39 g of the β-carboxyethyl ether of dimethyl-β-bromoethynylcarbinol and 20 ml of thionyl chloride was heated for 30 minutes at 60-65° in a round-bottomed flask connected to a reflux condenser with a calcium chloride tube and distilled. We obtained 38.5 g (91%) of the acid chloride of the β-carboxyethyl ether of dimethyl-β-bromoethynylcarbinol (X, R = R' = CH₃).

B.p. 98-99° (7 mm), n^{20}D 1.4827, d^{20}_4 1.3993, MR_D 51.71. $C_8H_{10}O_2ClBr$. Calculated 51.73.

Similary, 27 g of the β-carboxyethyl ether of 1-(β-bromoethynyl)-cyclohexanol-1 and 15 ml of thionyl chloride yielded 25.8 g (90%) of the acid chloride of the β-carboxyethyl ether of 1-(β-bromoethynyl)-cyclo-hexanol-1 [X, RR' = (CH₂)₅].

B.p. 106-108° (1 mm), n^{20}D 1.5090, d^{20}_4 1.3740, MR_D 63.78. $C_{11}H_{14}O_2ClBr$. Calculated 63.40

Reaction of Acid Chlorides of β-Carboxyethyl Ethers [X, R = R' = CH$_3$ and RR' = (CH$_2$)$_5$] with Ammonia

100 ml of dry ether was stirred at 5° and saturated with dry ammonia. 34.3 g of the acid chloride of the β-carboxyethyl ether of dimethyl-β-bromoethynylcarbinol was added with stirring over a period of an hour to the solution obtained at 5-10°; simultaneously a stream of gaseous ammonia was passed through. The reaction mixture was stirred in an atmosphere of ammonia at 5-10° for a further 2 hours. The precipitate was filtered off and washed on the filter with anhydrous acetone. The filtrate was evaporated in vacuum. We obtained 31.6 g (98%) of the amide of the β-carboxyethyl ether of dimethyl-β-bromoethynylcarbinol (XI, R = R' = CH$_3$) with m.p. 82-83° (from benzene).

Found %: N 5.94, 6.02. C$_8$H$_{12}$O$_2$NBr. Calculated %: N 5.98

Similarly, 22 g of the acid chloride of the β-carboxyethyl ether of 1-(β-bromoethynyl)-cyclohexanol-1 yielded 20.4 g (99%) of the amide of the β-carboxyethyl ether of 1-(bromoethynyl)-cyclohexanol-1 [XI, RR' = (CH$_2$)$_5$] with m. p. 108-110° (from benzene).

Found %: N, 5.01, 5.02. C$_{11}$H$_{16}$O$_2$NBr. Calculated %: N 5.11.

SUMMARY

The amides of the β-carboxyethyl ethers of dimethyl-β-bromoethynylcarbinol and 1-(β-bromoethynyl)-cyclohexanol-1 were synthesized with high yields at all the stages.

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THE PREPARATION OF CARBAMATES OF TERTIARY
ACETYLENE ALCOHOLS

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In recent years acetylene alcohols and their carbamates have occupied a prominent position among substances having a soporific or sedative effect. In this conncetion it is especially important to note the tertiary acetylene alcohols and their carbamates, in particular, the carbamate of 1-ethynylcyclohexanol-1, which is also known under the names of "Valamin" [1], "Valamid" and "Ethinamate" [2]. However, the preparation of esters of carbamic acid and tertiary acetylene alcohols involves considerable difficulties.

Despite the fact that there is a series of methods [3, 4], for the preparations of carbamates of alcohols in general, up to 1955 there was no method described in the literature for preparing the urethans of tertiary acetylene alcohols, despite reports of pharmacological tests of such compounds [1, 2, 5, 6]. It was only in 1955, when the experimental part of our work was completed, that two reports appeared on the synthesis of carbamates of tertiary acetylene alcohols.

In one of these reports [7], a description was given of the reaction of appropriate alcohols with $ClCOOC_6H_5$ in the presence of pyridine and treatment of the reaction product with liquid ammonia. In the second [8], the reaction of tertiary acetylene alcohols with isocyanates was reported.

Our attempts to prepare the carbamate of dimethylethynylcarbinol by reaction with urea, urea nitrate and also with phosgene and ammonia were unsuccessful; we were also unable to prepare the N-phenylcarbamate of dimethylethynylcarbinol by reaction with phenylisocyanate.

We synthesized the urethans of tertiary acetylene alcohols by Lester's method [3], which consists of treating the K-alcoholate or the O-MgBr derivative of the alcohol with phosgene and subsequent treatment of the reaction product with ammonia.
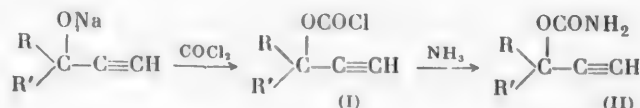
The chlorocarbonic acid derivatives (I) were not isolated, but were treated directly with gaseous ammonia. Urethan (II)(R = R' = CH₃) was also prepared, but in lower yield, by the reaction of phosgene with the K-alcoholate of dimethylethynylcarbinol, formed in the condensation of acetone with acetylene by A. E. Favorskii's method, and subsequent treatment with ammonia
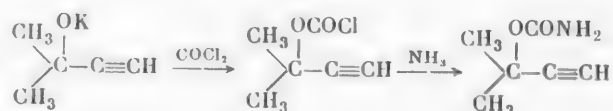
At the same time, it was not possible to prepare the required carbamate (II) (R = R' = CH₃) by the reaction of phosgene with $(CH_3)_2C(OMgBr)C \equiv CH$ and subsequent ammonolysis.

By using primary and secondary amines instead of ammonia, we were able to prepare N-substituted ureth-ans of dimethylethynylcarbinol.

$$\underset{CH_3}{\overset{CH_3}{>}}\underset{}{\overset{ONa}{\underset{|}{C}}}-C\equiv CH \xrightarrow{COCl_2} \underset{CH_3}{\overset{CH_3}{>}}\underset{}{\overset{OCOCl}{\underset{|}{C}}}-C\equiv CH \xrightarrow{R'R''NH} \underset{CH_3}{\overset{CH_3}{>}}\underset{}{\overset{OCONR'R''}{\underset{|}{C}}}-C\equiv CH$$
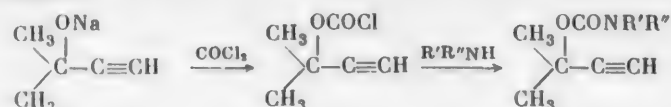
We studied the reactions of the Na-alcoholate and the $O-MgBr$ derivative of dimethyl-(vinylethynyl)-carbinol with phosgene and ammonia and isolated from the reaction mixture the dehydration product of the original alcohol — 2-methylhexadiene-1,5-yne-3 [9]. Evidently, the dehydration of the dimethyl-(vinylethynyl)-carbinol was the reason why we did not obtain the desired product — the urethan.

Results of phamacological tests. * The urethan of 1-ethynylcyclohexanol-1 [II, RR' = $(CH_2)_5$] has a sopori-fic action in amounts of 250 mg/kg (in white mice), ~ 200 mg/kg (in rats) and 500 mg/kg (in rabbits); the lethal dose is 537 mg/kg; in addition, this urethan increases the anesthetic effect of novocaine. The action of the urethan of 1-ethynylcyclopentanol-1 [II, RR' = $(CH_2)_4$] is similar to the action of the previous preparation; the lethal dose is 530 mg/kg. The urethans of dimethylethynylcarbinol (II, R = R'=CH_3) and methylethylethynyl-carbinol (II, R = CH_3, R' = C_2H_5) do not possess noticeable activity as soporifics.

EXPERIMENTAL

Carbamate of dimethylthynylcarbinol (II, R = R' = CH_3). a) Into a three-necked flask fitted with a mechanical stirrer and a thermometer was placed a mixture of 18.5 g of dimethylethynylcarbinol (b. p. 102-104°) and 250 ml of toluene. With stirring, 4.6 g of sodium in the form of small pieces was gradually intro-duced, while the temperature of the mixture was kept below 40° with external cooling; the reaction mixture was stirred until the sodium dissolved completely. The solution obtained was added over a period of 30 minutes with stirring to 170 ml of a 20% solution of phosgene in toluene in a four-necked flask, fitted with a mechanical stirrer, a thermometer, a reflux condenser and a dropping funnel; the temperature of the mixture rose to 60° due to heat evolution and then gradually fell to room temperature. The mixture was stirred for 1 hour at room tempterature, the dropping funnel replaced by a gas inlet tube and the excess phosgene flushed out with steam of air with stirring. Stirring was continued and gaseous ammonia passed in to complete saturation, while the tem-perature of the reaction mixture was kept below 30° with cooling. The precipitate formed was filtered off and carefully washed on the filter with toluene, the toluene solutions combined and evaporated in a water-pump vacuum and the residue fractionated. We obtained 13.1 g of a substance boiling at 125-150° (60 mm), which crystallized on standing . Recrystallization from benzine yielded 7.6 g (30%) of the carbamate of dimethyl-ethynylcarbinol with m.p. 93-95°.

Found %: N 11.30, 11.40. $C_6H_9O_2N$. Calculated %: N 11.02.

b) A mixture of 18 g of powdered potassium hydroxide and 250 ml of toluene was loaded into a 1.5 liter reactor, the air flushed from the reactor with nitrogen, which in its turn was flushed out with acetylene, acetyl-ene passed in to a pressure of 5 atmospheres and a solution of 14 g of acetone in 50 ml of toluene added from a dropper with stirring over a period of 40 minutes, while the acetylene pressure was kept at 5 atm. The mix-ture was stirred for 1 hour under a pressure of acetylene and then the toluene solution poured with stirring at 10° into 150 ml of a 20% solution of phosgene in toluene over a period of 30 minutes; the reaction mixture was stirred for 3 hours at 40-45° and left overnight. The next day the excess phosgene was flushed out with air with stirring and gaseous ammonia passed in at 20-30° for 2 hours. The precipitate was filtered off and washed on the filter with toluene. The toluene solution was evaporated under reduced pressure to leave 3.7 g of residue. Recrystallization from isooctane yielded 1.8 g (6%) of the carbamate of dimethylethynylcarbinol with m.p. 92-95°.

Carbamate of methylethylethynylcarbinol (II, R = CH_3, R' = C_2H_5). The reaction was similar to the pre-vious experiment. From 20 g of methylethylethynylcarbinol (b.p. 119-120°) and 4.6 g of sodium in 200 ml of

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*The pharmacological tests were carried out in the Pharmacological section of the S. Ordzhonikidze All-Union Scientific Research Institute of Chemical Pharmaceutics under the direction of M. D. Mashkovskii.

toluene and 170 ml of a 20% toluene solution of phosgene we obtained 8.2 g of a substance with b.p. 110-140° (16 mm), which crystallized on standing. Recrystallization from benzine yielded 5.2 g (18%) of the carbamate of methylethylethynylcarbinol with m.p. 54-56.5° [7].

Found %: N 10.00, 10.20. $C_7H_{11}O_2N$. Calculated %: N 9.93.

Carbamate of 1-ethynylcyclohexanol-1 [II, R, R' = $(CH_2)_5$]. A mixture of 15 g of 1-ethynylcyclohexanol-1 (b.p. 83-85° at 25 mm), 250 ml of toluene and 2.76 g of sodium was stirred at 40-50° until the sodium dissolved completely. The mixture obtained was gradually added at room temperature with stirring to 90 ml of a 20% toluene solution of phosgene and the reaction mixture stirred for 1 hour at room temperature and for 30 minutes at 50-60°. The excess phosgene was flushed out with a stream of air and a stream of ammonia passed in for 1.5 hours with stirring, while the temperature of the mixture was not more than 40°. The precipitate was filtered off and wahsed on the filter with hot ethyl acetate. The filtrate and wash solutions were combined and evaporated in a water-pump vacuum and the residue fractionated. We obtained 7.8 g of a substance with b.p. 150-170° (13 mm), which crystallized in the receiver. Recrystallization from benzine yielded 5.3 g (20%) of the carbamate of 1-ethynylcyclohexanol-1 with m.p. 96-96.5° [5].

Found %: N 8.48, 8.62. $C_9H_{13}O_2N$. Calculated %: N 8.38.

Carbamate of 1-ethynylcyclopentanol-1 [II, R, R' = $(CH_2)_4$]. A mixture of 22 g of 1-ethynylcyclopentanol-1 (b.p. 52-54° at 7 mm) and 4.6 g of sodium in 250 ml of toluene was stirred for 4 hours at 20-40° until the sodium dissolved completely. The mixture obtained was added with stirring at 20-30° to 170 ml of a 20% toluene solution of phosgene and then the mixture was stirred at room temperature for 3 hours and left overnight. The next day the excess phosgene was flushed out with a stream of air for 1 hour with stirring and ammonia passed in with stirring for 2 hours. The precipitate was filtered off and washed on the filter with toluene. The combined toluene solutions were evaporated in a water-pump vacuum and the residue fractionated. We obtained 8.2 g of a fraction with b.p. 120-150° (4 mm), which crystallized in the receiver. Recrystallization from benzine yielded 4.7 g (18%) of the carbamate of 1-ethynylcyclopentanol-1 with m.p. 117-118°.

Found %: N 9.51, 9.53. $C_8H_{11}O_2N$. Calculated %: N 9.15.

Carbamate of methyl-n-octylethynylcarbinol (II, R = CH_3, R' = C_8H_{17}). A mixture of 18.2 g of methyl-n-octylethynylcarbinol (b.p. 136° at 19 mm) and 2.3 g of sodium in 250 ml of toluene was stirred at 40-50° for 1 hour. The solution formed was poured with stirring into 100 ml of a 20% toluene solution of phosgene, stirring was continued for 2 hours and the mixture left overnight and then stirred for a further 30 minutes at 40-50°. Working up in the usual way yielded 5.7 g of a fraction with b.p. 120-135° (0.5 mm). Recrystallization from benzine gave 2.6 g (11.5%) of the carbamate with m.p. 67-69°.

Found %: N 6.62, 6.78. $C_{13}H_{23}O_2N$. Calculated %: N 6.44.

N-Substituted Carbamates of Dimethylethynylcarbinol

1. N-Methylcarbamate. To 150 ml of a 20% toluene solution of phosgene was added a mixture obtained from 4.6 g of sodium and 17 g of dimethylethynylcarbinol in 250 ml of toluene. The mixture was stirred for 30 minutes at 50°, cooled and the excess phosgene flushed out with air. Excess gaseous methylamine was passed in at 20-30° with stirring and the precipitate filtered off and washed on the filter with toluene. The toluene was removed under reduced pressure and the residue crystallized on standing. We obtained 2.3 g (8%) of the N-methylcarbamate of dimethylethynylcarbinol with m.p. 68-70° (from benzine).

Found %: N 9.74, 9.75. $C_7H_{11}O_2N$. Calculated %: N 9.93.

2. N,N-Dimethylcarbamate. A mixture of 150 ml of a 20% toluene solution of phosgene and a solution obtained from 4.6 g of sodium and 17 g of dimethylethynylcarbinol in 250 ml of toluene was stirred for 6 hours at room temperature, left overnight and stirred for a further 30 minutes at 40-50°. The excess phosgene was flushed out and excess gaseous dimethylamine passed in, the precipitate filtered off and washed on the filter with toluene, the toluene removed and the residue fractionated several times. We obtained 4.3 g (14%) of the N,N-dimethylcarbamate of dimethylethynylcarbinol with b.p. 73-77° (8 mm) n_D^{20} 1.4497.

Found %: N 9.30, 9.41. $C_8H_{13}O_2N$. Calculated %: N 9.03.

3. N,N-Diethylcarbamate. A mixture of 150 ml of a 20% toluene solution of phosgene and a solution obtained from 4.6 g of sodium and 17 g of dimethylethynylcarbinol in 250 ml of toluene was stirred for 2 hours at room temperature and for 2 hours at 40-50°. When the excess phosgene had been flushed out, 35 g of diethylamine was added and the mixture stirred for 3 hours, left overnight and treated as usual. Several distillations yielded 8.7 g (24%) of the N,N-diethylcarbamate of dimethylethynylcarbinol with b. p. 88-91° (8 mm), n_D^{20} 1.4468.

Found %: N 7.87, 7.93. $C_{10}H_{17}O_2N$. Calculated %: N 7.65.

4. N-Piperidylcarbamate. A mixture of 150 ml of a 20% toluene solution of phosgene and a solution obtained from 4.6 g of sodium and 17 g of dimethylethynylcarbinol in 250 ml of toluene was stirred for 2 hours at room temperature and left for 2 days. After removal of the excess phosgene, 35 g of piperidine was added and the mixture stirred at room temperature for 2 hours, left overnight and treated as usual. Several distillations yielded 6.3 g (16%) of the N-piperidylcarbamate of dimethylethynylcarbinol with b. p. 70-83° (8 mm), n_D^{20} 1.4721.

Found %: N. 7.49, 7.38. $C_{11}H_{17}O_2N$. Calculated %: N 7.18.

5. N-Phenylcarbamate. As in the previous experiment, from a mixture of a solution obtained from 4.6 g of sodium and 17 g of dimethylethynylcarbinol in 250 ml of toluene, 150 ml of a 20% toluene solution of phosgene and 55 g of aniline, we obtained 15.4 g of a fraction boiling at 136-150° (11 mm), which crystallized in the receiver. Recrystallization from benzine yielded 7.3 g (18%) of the N-phenylcarbamate of dimethylethynylcarbinol with m.p. 100.5-101° [10].

Found %: N 7.19, 7.03. $C_{12}H_{13}O_2N$. Calculated %: N 6.90.

SUMMARY

1. A study was made of the reaction of the Na-alcoholates of tertiary acetylene alcohols with phosgene and ammonia or primary and secondary amines and the possibility of preparing carbamates of tertiary acetylene alcohols in this way was demonstrated.

2. A series of carbamates of tertiary acetylene alcohols was prepared.

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SYNTHESIS OF STEROID COMPOUNDS AND RELATED SUBSTANCES

44. REDUCTION OF 9-METHYL-1-ETHYNYL-1-HYDROXY-6-KETO-Δ5-OCTALIN AND ITS DERIVATIVES WITH SODIUM BOROHYDRIDE

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The reduction of ketosteroids to the corresponding alcohols has been widely studied. Recently there has been an increasing application of complex metal hydrides of the type $MeAlH_4$, $MeBH_4$, and $MeH(BOR)_3$ in this field.

One of the mildest and most conveniently handled reagents of this type is $NaBH_4$, by means of which it is possible to reduce ketones selectively and stereoselectively [1].

In a previous report we described the selective reduction of 9-methyl-1-ethynyl-1-hydroxy-6-keto-Δ5-octalin (I) and its derivatives with lithium in liquid ammonia and their catalytic hydrogenation [2]. In order to prepare intermediates in the synthesis of steroids, in the present work a study was made of the reduction of the keto alcohols (I-VI) with sodium borohydride. As in the reduction of 9-methyl-1,6-diketo-Δ5-octalin with $NaBH_4$ [3], the reduction was performed in dilute alcohol solutions with cooling and stirring. This gave good yields of the corresponding crystalline alcohols (VII-XII) with the same steric configuration of the hydroxyl group at C_6, which was demonstrated by hydrogenation of these alcohols into the same known diol (X), which we synthesized previously by catalytic hydrogenation of the alcohols (I) and (XI). The latter was obtained by reduction of the keto alcohol (II) with lithium in liquid ammonia in the presence of alcohol, which, as is known, leads to compounds with an equatorial orientation of the alcohol group, even in the reduction of such sterically hindered ketones as 11-keto steroids [4].

Slow reduction of sterically unhindered ketones of the 3-keto steroid type with complex hydrides also leads to the predominant formation of the most stable compounds with an equatorial configuration of the hydroxy groups [5, 6].

Thus, in the alcohols (VII-XII) we obtained, the secondary alcohol groups must occupy an equatorial position.

Acetylation of the diols (VII-XII) with acetic anhydride in pyridine proceeded selectively and formed the corresponding 6-monoacetates (XIII-XVIII). The tertiary hydroxyl at C1 was not acetylated under more drastic conditions either. Thus, when the keto alcohol (II) was heated with acetic anhydride in pyridine or treated with acetyl chloride in pyridine, the original alcohol was recovered.

When the acetylene keto alcohol (XIX) [7] was reduced with sodium borohydride under the conditions described above, the two isomeric diols (XX) and (XXI) were formed. In this case the low-boiling isomer (XX) predominated. Exhaustive hydrogenation of the high-boiling isomer (XXI) over platinum oxide gave the known ethyldiol (XXII), which we prepared previously by reduction of the corresponding ketol with lithium in liquid ammonia.
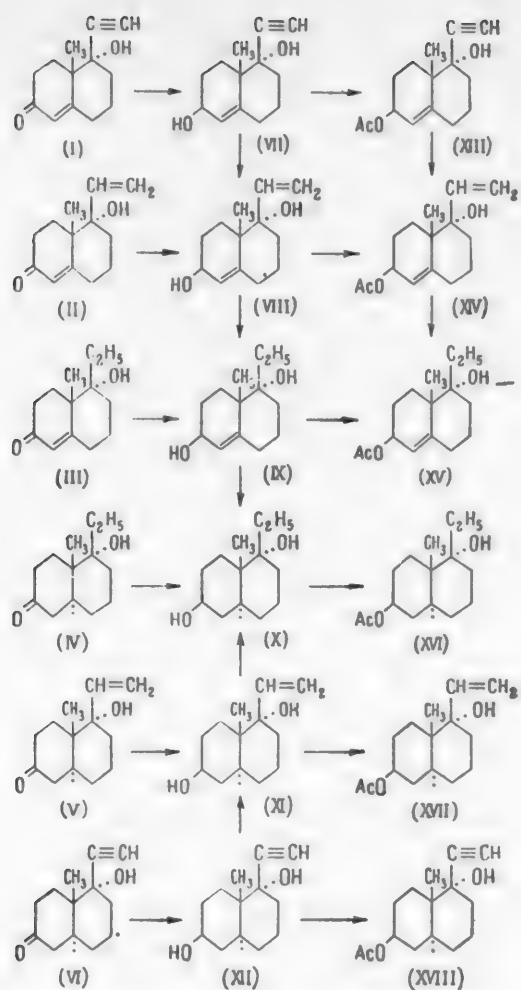
Consequently, in the diols (XXI) and XXII, the secondary hydroxyl group is disposed equatorially with respect to the ring and in the alcohol (XX) it is axial. The predominant formation of the diol (XX) in the reduction of the keto alcohol (XIX) with sodium borohydride is explained by the fact that the keto alcohol is a derivative of cis-decalin and $NaBH_4$ attacks the keto group in this case predominantly from the equatorial region since the approach of such a bulky reagent from the axial region must be hindered. In its turn, this direction of the reduction of the ketone (XIX) indicates that it reacts in an alcohol solution mainly in conformation (a) with an axial disposition of the angular methyl group.
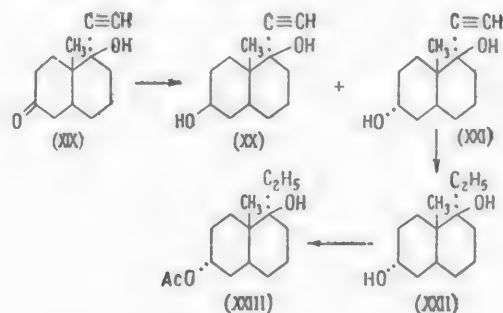
This reasoning is confirmed by the fact that reduction of unsubstituted 9-methyl-3-ketodecalin with LiAlH$_4$ gives an alcohol with an axially disposed hydroxyl group at C$_3$ [8]. The formation of the isomer (XXI) apparently proceeds from the other possible conformation of the ketone (XIX), to which conformation (b) refers.

Acetylation of the diol (XXII) under the conditions described above also gives the 6-monoacetate (XXIII).

As we showed previously, hydrogenation of ketol (I) in alcohol over platinum oxide forms the diol (X). The saturated keto alcohol (IV) is not an intermediate in this reaction since it is not hydrogenated under the given conditions. Another possible intermediate in this reaction could be the diol (IX), prepared in the present work. However, as was found, the isolated double bond in diol (IX), as in acetate (XV), is hardly hydrogenated in alcohol solutions in the presence of platinum or palladium catalysts. Diol (IX) can be hydrogenated in acetic acid over platinum oxide, when diol (X) is formed in noticeable amounts. Thus, diol (IX) is also not an intermediate in this reaction. Consequently, the production of diol (X) in the hydrogenation of the keto alcohol (I) may be explained by an increase in the reactivity of the intermediates under direct contact with the catalyst. This intermediate reaction product may be the enol form of ketone (IV), initially formed by hydrogenation of the keto alcohol (I) or its enol form.
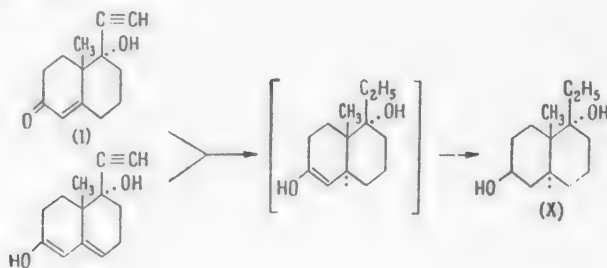
EXPERIMENTAL

Reduction with Sodium Borohydride

In all cases a preparation containing 85 % NaBH$_4$ was used. All the substances obtained were dried by heating in vacuum over P$_2$O$_5$.

9-Methyl-1-ethynyl-1,6-dihydroxy-Δ5-octalin (VII). 1.4 g of the acetylene keto alcohol (I) was dissolved in a mixture of 20 ml of alcohol and 10 ml of dioxane. 400 mg of NaBH$_4$ was added in portions to the solution, which was stirred and cooled in ice water. Stirring was continued for a further 3 hours. The next day the excess reagent was decomposed with a few drops of acetic acid. The solution was evaporated to dryness in vacuum and water added. The crystalline product was filtered, washed with water and dried. We obtained 1.17 g of diol (VII) with m.p. 155-155.5° (from acetone).

Found %: C 76.00, 76.12; H 8.81, 8.98. C$_{13}$H$_{18}$O$_3$. Calculated %: C 75.69; H 8.80.

Similarly, 1 g of keto alcohol (II) yielded 0.85 g of trans-9-methyl-1-vinyl-1,6-dihydroxy-Δ5-octalin (VIII) with m.p. 152-153° (from acetone).

Found %: C 74.84; 74.91; H 9.96, 9.93. C$_{13}$H$_{20}$O$_2$. Calculated %: C 74.92; H 9.68.

From 1.75 g of the keto alcohol (III) we obtained 1.45 g of trans-9-methyl-1-ethyl-1,6-dihydroxy-Δ5-octalin (IX) with m.p. 158-159°(from acetone).

Found %: C 74.25, 74.24; H 10.47, 10.55. $C_{13}H_{22}O_2$. Calculated %: C 74.20; H 10.54.

From 0.12 g of ketone (IV) we obtained 80 mg of 9-methyl-1-ethyl-1,6-dihydroxydecalin (X) with m.p. 155-156° (a mixed melting point with an authentic sample was not depressed).

From 0.6 g of keto alcohol (V) we obtained 0.5 g of trans-9-methyl-1-vinyl-1,6-dihydroxydecalin (XI) with m.p. 137-138° (a mixed melting point with an authentic sample was not depressed).

From 0.34 g of keto alcohol (VI) we obtained 300 mg of trans-9-methyl-1-ethynyl-1,6-dihydroxydecalin (XII) with m.p. 192-193° (from a mixture of acetone and alcohol).

Found %: C 74.67, 74.60; H 9.55, 9.68. $C_{13}H_{20}O_2$. Calculated %: C 74.96; H 9.68.

From 0.35 g of keto alcohol (XIX) we obtained 120 mg of cis-9-methyl-1-ethynyl-1,6-dihydroxydecahydro-naphthalene (XX) with m.p. 109-110° (from ether).

Found %: C 75.20, 75.25; H 9.50, 9.66. $C_{13}H_{20}O_2$. Calculated %: C 74.96; H 9.68.

In addition, we isolated a further 90 mg of the stereoisomer (XXI) with m. p. 155-156° (from acetone).

Found %: C 75.09, 74.96; H 9.71, 9.66. $C_{13}H_{20}O_2$. Calculated %: C 74.96; H 9.68.

Acetylation of Diols

6-Acetate of diol (VII). 1.1 g of diol (VII) was dissolved in a mixture of pyridine and acetic anhydride. The next day the solvent was distilled off in vacuum. Water was added. 0.9 g of crystals of the 6-acetate (XIII) with m. p. 110-111° (from ether) was collected.

Found %: C 72.90, 73.01; H 8.22, 8.10. $C_{15}H_{20}O_3$. Calculated %: C 72.55; H 8.12.

Similarly, diol (XI) yielded 6-acetate (XVII) with m. p. 122-123° (from ether).

Found %: C 71.01, 70.87; H 9.54, 9.52. $C_{15}H_{24}O_3$. Calculated %: C 71.39; H 9.59.

The rest of the acetates were isolated by extraction with ether and chromatography on aluminum oxide.

1.9 g diol (VIII) yielded 1.6 g of the 6-acetate (XIV) with m.p. 78-79° (from ether.).

Found %: C 71.53; H 8.88. $C_{15}H_{22}O_3$. Calculated %: C 71.96; H 8.85.

Diol (IX) gave the 3-acetate (XV) with m.p. 75-76° (from ether).

Found %: C 71.05, 70.89; H 9.25, 9.36. $C_{15}H_{24}O_3$. Calculated %: C 71.39; H 9.59.

Diol (X) gave the 6-acetate (XVI) with m.p. 60.5-61.5° (from ether).

Found %: C 71.23; 71.21; H 10.20, 10.00. $C_{15}H_{26}O_3$. Calculated %: C 70.83; H 10.31.

Diol (XII) gave the 6-acetate (XVIII) with m.p. 86-87° (from ether with petroleum ether).

Found %: C 71.62, 71.52; H 8.82, 8.83. $C_{15}H_{22}O_3$. Calculated %: C 71.96; H 8.85.

Diol (XXI) gave the 3-acetate (XXIII) with m.p. 57-58° (from ether with petroleum ether).

Found %: C 70.88, 70.84; H 10.27, 10.32. $C_{15}H_{26}O_3$. Calculated %: C 70.83; H 10.31.

Hydrogenation

1) 0.5 g of the acetylene diol (VII) was exhaustively hydrogenated in alcohol in the presence of platinum oxide (120 ml of H_2 was absorbed). Removal of the solvent and three recrystallizations from acetone yielded crystals with m.p. 153-154°. A mixture with the unsaturated ethyldiol (IX) had an intermediate melting point. A mixture with the saturated ethyldiol (X) melted at 148-149°.

2) In the hydrogenation of 200 mg of the vinyldiol (VIII) uner the same conditions, 25 ml of H_2 was absorbed and the hydrogenation was stopped. We obtained the ethyldiol (IX).

3) Exhaustive hydrogenation of diol (XII) gave the ethyldiol (X).

4) Hydrogenation of the diol (XXI) gave diol (XXII).

5) 300 mg of the ethyldiol (IX) was exhaustively hydrogenated in acetic acid over platinum oxide. About 50 ml of hydrogen was absorbed. Removal of the solvent yielded 100 mg of crystals with m.p. 155-156°. A mixed melting point with the saturated diol (X) was not depressed.

Hydrogenation of acetates. 480 mg of the 6-acetate (XIII) was hydrogenated in dioxane with a Pd-catalyst. 54 ml of hydrogen was slowly absorbed and the hydrogenation discontinued. (A test for an acetylene with an ammonia silver complex was negative). We obtained a crystalline substance with m.p. 74-75° (from ether). A mixed melting point with the 6-acetate of the vinyldiol (XIV) was not depressed. On further hydrogenation of the vinylacetate (XIV) in alcohol in the presence of platinum oxide 52 ml of hydrogen was absorbed and the hydrogenation stopped. We obtained the acetate of an ethyldiol. A mixed melting point with an authentic sample of (XV) was not depressed.

SUMMARY

1. It was shown that the reduction of 1-ethynyl-, 1-vinyl- and 1-ethyl-substituted 9-methyl-1-hydroxy-Δ5-6-ketooctalins and 1-ethynyl-, 1-vinyl- and 1-ethyl-substituted 9-methyl-1-hydroxy-6-ketodecalins with sodium borohydride gave good yields of the corresponding diols with an equatorial disposition of the secondary alcohol group.

2. The selective acetylation of the diols listed into the corresponding 6-monoacetates was accomplished.

3. A mechanism is put forward for the hydrogenation of Δ5-6-ketooctalol.

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PIPERIDINE DERIVATIVES AS POSSIBLE HYPOTENSIVE DRUGS

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In a previous communication [1] it was shown that some secondary-tertiary amines of the quinuclidine and piperidine series possess a high ganglioblocking activity. For further study of tertiary amines as possible ganglioblocking agents, some N-substituted piperidine derivatives, which are described in the present work, were synthesized. The starting material for their synthesis was 2,6-lutidine, a waste product from the production of phthivazide.

On reacting 2,6-lupetidine, obtained from 2,6-lutidine, with β-chloropropionyl chloride and then boiling the reaction product with piperidine and diethylamine in anhydrous ethyl alcohol, we obtained 1-[β-(N-piperidino)-propionyl]-2,6-dimethylpiperidine (I) and 1-(β-diethylaminopropionyl)-2,6-dimethylpiperidine (II). Reduction of these compounds with lithium aluminum hydride yielded 1-[γ-(N-piperidino)-propyl]-2,6-dimethylpiperidine (III) and 1-(β-diethylaminopropyl)-2,6-dimethylpiperidine (IV).

(I) R = COCH$_2$CH$_2$ N⟨ ⟩

(II) R = COCH$_2$CH$_2$N(C$_2$H$_5$)$_2$

(III) R = CH$_2$CH$_2$CH$_2$ N⟨ ⟩

(IV) R = CH$_2$CH$_2$CH$_2$N(C$_2$H$_5$)$_2$
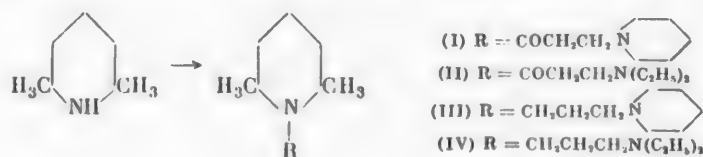
Attempts to prepare the diquaternary salts by reacting 2,6-lutidine and 1,2,6-trimethylpiperidine with 1,5-dibromopentane and 1,6-dibromohexane did not give the desired result. Heating the components in boiling anhydrous alcohol, in a alcohol and benzene in tubes at 150° and in tubes without solvent yielded only the hydrobromides of the original 2,6-lutidine and 1,2,6-trimethylpiperidine.

Diquaternary salts were syntesized starting from 2,6-lupetidine, using the diacid chlorides of glutaric and adipic acids. Reaction of the latter with excess 2,6-lupetidine in anhydrous ether yielded the bis(2,6-dimethylpiperidide) of glutaric acid (V) and the bis(2,6-dimethylpiperidide) of adipic acid (VI). The latter were reduced with lithium aluminum hydride to 1,5-bis(2'6'-dimethylpiperidino-1'-)-pentane (VII) and 1,6-bis(2',6'-dimethylpiperidino-1')-hexane (VIII). Compounds (VII) and (VIII) were readily converted into diquaternary salts.

(V) n = 3,
(VI) n = 4.

(VII) n' = 5,
(VIII) n' = 6.
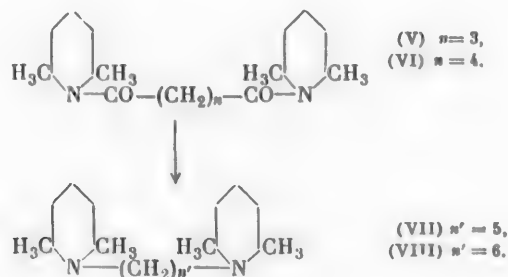
Reaction of the ethyl ether of 6-methylpipecolinic acid with β-chloropropionyl chloride in anhydrous benzene with subsequent treatment of the reaction product with piperidine or diethylamine yielded 1-[β-(N-piperidino) -propionyl]-2-carbethoxy-6-methylpiperidine (IX) and 1-(β-diethylaminopropionyl)-2-carbethoxy-6-methylpiperidine (X). Reduction of these compounds with lithium aluminum hydride led to 1-[γ-(N-piperidino)-propyl]-2-hydroxymethyl-6-methylpiperidine (XI) and 1-(γ-diethylaminopropyl)-2-hydroxymethyl-6-methylpiperidine (XII), respectively.
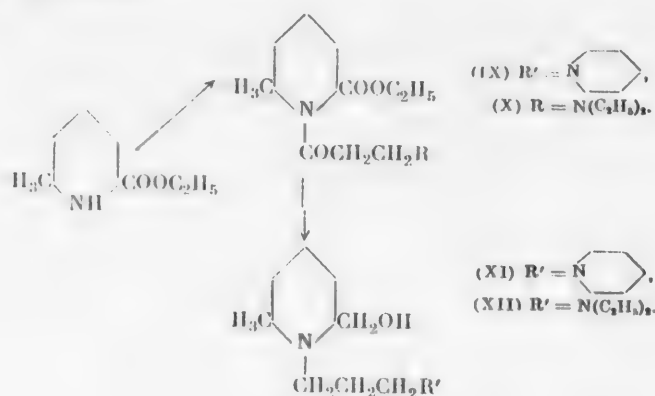
The results of testing the compounds obtained will be published later.

EXPERIMENTAL

1-[β-(N-Piperidino)-propionyl]-2,6-dimethylpiperidine (I). 6.17 g of β-chloropropionyl chloride and a solution of 1.94 g of sodium hydroxide in 4 ml of water were added simultaneously with stirring to a solution of 5 g of 2,6-lupetidine in 15 ml of water, cooled to −5°. After the addition, the reaction mixture was stirred at 5° for 15 minutes and then at room temperature for 2 hours. The reaction solution was made alkaline with excess 50% potassium carbonate solution and extracted with ether. The ether extract was dried with baked sodium sulfate and the ether evaporated. We obtained 5.87 g (65.2%) of technical 1-(β-chloropropionyl)- 2,6-dimethylpiperidine as a yellowish, mobile liquid. The latter was dissolved in 30 ml of anhydrous ethyl alcohol, 4.9 g of piperidine added and the solution boiled for 5 hours. The alcohol was then removed in vacuum and the residue treated with excess 50% potassium carbonate solution and extracted with ether. The ether extract was dried with anhydrous sodium sulfate, the ether removed and the residue vacuum distilled. We obtained 2.25 g (71.5%) of 1-[β-(N-piperidino)-propionyl]-2,6-dimethylpiperidine with b.p. 149-151° (0.3 mm) as a colorless sirupy liquid, which was readily soluble in the normal organic solvents.

The hydrochloride was a white crystalline substance with m.p. 200-202° (from alcohol).

Found %: N 10.07; Cl 12.28. $C_{15}H_{29}ON_2Cl$. Calculated %: N 9.70; Cl 12.30.

1-(β-Diethylaminopropionyl)-2,6-dimethylpiperidine (II). From 7.71 g of technical 1-(β-chloropropinyl)--2,6-dimethylpiperidine and 11 g of diethylamine in 38 ml of anhydrous ethyl alcohol, by the method described above we obtained 5.92 g (65.0%) of 1-(β-diethylaminopropionyl)-2,6-dimethylpiperidine as a colorless liquid with b.p. 136-138° (0.5 mm), which was soluble in the normal organic solvents.

Found %: C 69.51; H 11.55; N 11.73. $C_{14}H_{28}ON_2$. Calculated %: C 70.00; H 11.66; N 11.66.

The hydrochloride and the methiodide were oily materials.

1-[γ-(N-Piperidino)-propyl]-2,6-dimethylpiperidine (III). 5.25 g of 1-[β-(N-piperidino)-propionyl]-2,6-dimethylpiperidine was reduced with 1.58 g of lithium aluminum hydride in ether solution. We obtained 3.47 g (70%) of 1-[γ-(N-piperidino)-propyl]-2,6-dimethylpiperidine as a colorless mobile liquid with b.p. 117-120° (0.3 mm), which was readily soluble in normal organic solvents.

The dihydrochloride was an oily material. The dimethiodide formed white crystals with m.p. 204-206° (from alcohol).

Found %: N 5.26; I 48.05. $C_{17}H_{33}N_2I_2$. Calculated %: N 5.36; I 48.65.

1-(γ-Diethylaminopropyl)-2,6-dimethylpiperidine (IV). 7.32 g of 1-(β-diethylaminopropionyl)-2,6-dimethylpiperidine was reduced with 2.3 g of lithium aluminum hydride in ether. We obtained 4.23 g (61.3%) of 1-(γ-diethylaminopropyl)-2,6-dimethylpiperidine with b. p. 93-96° (0.4 mm), which was soluble in the normal organic solvents.

The dihydrochloride was an oily substance. The dimethiodide formed white crystals with m. p. 221-222° (from alcohol).

Found %: N 5.35; I 49.12. $C_{18}H_{36}N_2I_2$. Calculated %: N 5.49; I 49.80.

Bis(2,6-dimethylpiperidide) of glutaric acid (V). A solution of 5.5 g of 2,6-lupetidine in 20 ml of anhydrous ether was added dropwise at 10° to a solution of 1.63 g of the diacid chloride of glutaric acid in 15 ml of anhydrous ether. The mixture was stirred with cooling for 3 hours, then treated with excess 50% potassium carbonate solution and extracted with ether. The ether extract was dried with anhydrous sodium sulfate, the ether removed and the residue vacuum distilled. We obtained 2.33 g (74.4%) of the bis(2,6-dimethylpiperidide) of glutaric acid as a light yellow, caramel-like mass with b.p. 196° (0.25 ml), which was difficultly soluble in ether, but soluble in benzene, ethyl alcohol and chloroform.

Found %: C 70.56; H 10.41; N 8.69. $C_{19}H_{34}O_2N_2$. Calculated %: C 70.80; H 10.55; N 8.69.

Bis(2,6-dimethylpiperidide) of adipic acid (VI). From 5 g of the diacid chloride of adipic acid and 15.4 g of 2,6-lupetidine in 80 ml of anhydrous ether, by the method described above we obtained 6.18 g (67.3%) of the bis(2,6-dimethylpiperidide) of adipic acid with b.p. 126-130° (0.6 mm) as a light yellow spirit* which crystallized on standing, the crystals had m.p. 103-104°.

Found %: C 71.48; H 10.60; N 8.40. $C_{20}H_{36}O_2N_2$. Calculated %: C 71.42; H 10.71; N 8.33.

1,5-Bis(2',6'-dimethylpiperidino-1')-pentane (VII). 2 g of the bis(2,6-dimethylpiperidide) of glutaric acid was reduced with 0.71 g of lithium aluminum hydride in ether solution. We obtained 1.8 g (97.8%) of 1,5-bis(2',6'-dimethylpiperidino-1')-pentane with b.p. 176-177° (6 mm). The distilled product crystallized on cooling; the m.p. was 34-36°.

Found %: C 77.52; H 12.75; N 9.57. $C_{19}H_{38}N_2$. Calculated %: C 77.55; H 12.92; N 9.52.

The dimethiodide formed white crystals with m.p. 249-250° (from acetone).

Found %: N 4.83; I 43.54. $C_{21}H_{44}N_2I_2$. Calculated %: N 4.84; I 43.93.

1,6-Bis(2',6'-dimethylpiperidino-1')-hexane (VIII). 4.83 g of the bis(2,6-dimethylpiperidide) of adipic acid was reduced with 2.6 g of lithium aluminum hydride in an ether-benzene solution. We obtained 4.02 g (90.9%) of 1,6-bis(2',6'-dimethylpiperidino-1')-hexane with b.p. 196-197° (7 mm). When cooled, the mass crystallized; the m.p. was 66-68°.

Found %: C 78.14; H 12.80; N 8.85; N 8.85. $C_{20}H_{40}N_2$. Calculated %: C 77.92; H 12.98; N 9.09.

The dimethiodide formed white crystals with m.p. 240-241° (from acetone).

Found %: N 4.69; I 42.59. $C_{22}H_{46}N_2I_2$. Calculated %: N 4.72; I 42.90.

1-[β-(N-Piperidino)-propionyl]-2-carbethoxy-6-methylpiperidine (IX). 1.93 g of β-chloropropionyl chloride was added dropwise to 5.2 g of the ethyl ether of 6-methylpipecolinic acid, dissolved in 35 ml of anhydrous benzene and cooled with ice; the reaction mixture was then stirred for 3 hours, diluted with 60 ml of anhydrous ether and the precipitate (2.54 g) of the hydrochloride of ethyl 6-methylpipecolinate was filtered off. The filtrate was evaporated in vacuum. We obtained 2.76 g (70%) of technical 1-(β-chloropropionyl)-2-carbethoxy-6-methylpiperidine as a light yellow, sirupy liquid. The latter was dissolved in 20 ml of anhydrous

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*The Russian is probably incorrect and this word should probably be sirup – Translator's note.

alcohol 1.7 g of piperidine added and the mixture boiled for 5 hours. The alcohol was removed in vacuum, the residue treated with 50% potassium carbonate solution and extracted with ether, the extract dried with anhydrous sodium sulfate and the ether distilled off. The residue was vacuum distilled. We obtained 2.66 g (81.2%) of 1-[β-(N-piperidino)-propionyl]-2-carbethoxy-6-methylpiperidine with b.p. 170-172° (0.45 mm).

Found %: C 65.22; H 9.29; N 8.95. $C_{17}H_{30}O_3N_2$. Calculated %: C 65.80; H 9.67; N 9.03.

The hydrochloride was an oily liquid. The methiodide formed white crystals, which were extremely hygroscopic.

Found %: N 6.09, 6.01. $C_{18}H_{33}O_3N_2Cl$. Calculated %: N 6.19.

1-(β-Diethylaminopropionyl)-2-carbethoxy-6-methylpiperidine (X). From 2.5 g of technical 1-(β-chloropropionyl)-2-carbethoxy-6-methylpiperidine and 2.8 g of diethylamine in 20 ml of anhydrous ethyl alcohol we obtained, as described above, 2.01 g (70.7%) of 1-(β-diethylaminopropionyl)-2-carbethoxy-6-methylpiperidine with b.p. 144-146° (0.2 mm).

Found %: N 9.28; 9.47. $C_{16}H_{30}O_3N_2$. Calculated %: N 9.39.

1-[γ-(N-Piperidino)-propyl]-2-hydroxymethyl-6-methylpiperidine(XI). 1.68 g of 1-[β-(N-piperidino)-propionyl]-2-carbethoxy-6-methylpiperidine was reduced with 0.62 g of lithium aluminum hydride in ether solution. We obtained 0.92 g (67%) of 1-[γ-(N-piperidino)-propyl]-2-hydroxymethyl-6-methylpiperidine with b.p. 132-134° (0.2 mm). The substance was soluble in the usual organic solvents and water.

Found %: C 70.46; H 11.92; N 10.65. $C_{15}H_{30}ON_2$. Calculated %: C 70.86; H 11.81; N 11.02.

The dihydrochloride and the dimethiodide were oily substances.

1-(γ-Diethylaminopropyl)-2-hydroxymethyl-6-methylpiperidine (XII). 1.78 g of 1-(β-diethylamino-propionyl)-2-carbethoxy-6-methylpiperidine was reduced with 0.68 g of lithium aluminum hydride in ether solution. We obtained 1.11 g (77%) of 1-(γ-diethylaminopropyl)-2-hydroxymethyl-6-methylpiperidine with b.p. 127-129° (0.35 mm). The substance was soluble in the usual organic solvents and water.

Found %: N 11.14, 11.14. $C_{14}O_{30}ON_2$. Calculated %: N 11.57.

The hydrochloride and the methiodide were oily substances.

SUMMARY

Some N-substituted 2,6-lupetidines and ethyl 6-methylpipecolinates were synthesized so that their pharmacological activity could be studied.

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*Original Russian pagination. See C.B. Translation.

A STUDY OF THE FORMATION OF N-SUBSTITUTED
2-AMINOMETHYL-3-VINYLQUINUCLIDINES

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In previous communications [1, 2] we described the synthesis of various 2,3-disubstituted quinuclidines, including N-substituted 2-aminomethyl-3-(β-hydroxyethyl)-quinuclidine. The latter may be used as the starting material for synthesizing quinuclidine derivatives containing a vinyl group. The present article describes investigations on the possibility of converting N-substituted 2-aminomethyl-3-(β-hydroxyethyl)-quinuclidines into N-substituted 2-aminomethyl-3-vinylquinuclidines by distillation of the corresponding esters of stearic and benzoic acids at atomspheric pressure [3]. The esters were prepared by reacting the acid chlorides of stearic and benzoic acids with N-substituted 2-aminomethyl-3-(β-hydroxethyl)-quinuclidines in benzene solution. Distillation of 2-diethylaminomethyl-3-(β-stearyloxyethyl)-quinuclidine (I) yielded two substances – 2-diethylaminomethyl-3-vinylquinuclidine (II) and 2,3-(3',4'-N-ethylpiperidino)-quinuclidine (III), with the vinyl derivative representing about 10% of the total of the two substances. It was possible to separate (II) and (III) by treating the mixture with mercuric acetate in acetic acid with subsequent separation of the product by adding mercuric acetate to the unsaturated compound (II) and isolation of (II) by decomposing the addition product with phosphorous acid. Together with compounds (II) and (III) the reaction products from distillation of ester (I) yielded ethyl stearate, confirming that ester (I) is converted into the tricyclic compound (III) during this process. The formation of compound (II) is apparently accompanied by the liberation of stearic acid, but due to its small amount in the reaction products, the acid was not isolated.
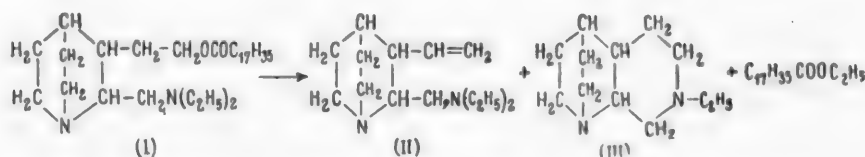
If 2-diethylaminomethyl-3-(β-benzoyloxyethyl)-quinuclidine (IV) was distilled at atmospheric pressure, then only the tricyclic derivative (III) and ethyl benzoate were formed. No substance containing a double bond was detected among the reaction products.
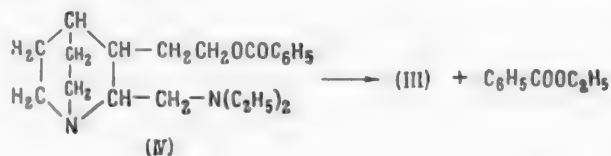
A similar process was observed when 2-ethylaminomethyl-3-(β-benzoyloxyethyl)-quinuclidine (V) was heated to its boiling point. In this case, benzoic acid was isolated together with 2,3-(3',4'-N-ethylpiperidino)--quinuclidine (III).

$$\text{(V)} \longrightarrow \text{(III)} + C_6H_5COOH$$
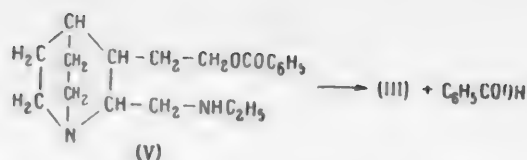
Heating both 2-dimethylaminomethyl-3-(β-hydroxyethyl)-quinuclidine (VI) and 2-ethylaminomethyl--3-(β-hydroxyethyl)-quinuclidine (IX) with phthalic anhydride in the presence of benzenesulfonic acid [4] at 285° gave only compound (III).
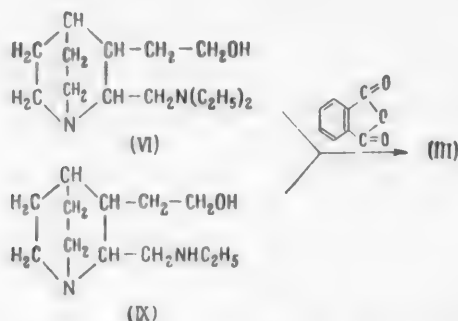
The structure of 2,3-(3',4'-N-ethylpiperidino)-quinuclidine, formed by distillation of esters of 2-diethyl-(ethyl)-aminomethyl-3-(β-hydroxyethyl)-quinuclidine at atmospheric pressure and also by heating 2-diethyl-(ethyl)-aminomethyl-3-(β-hydroxyethyl)-quinuclidines with phthalic anhydride in the presence of benzenesulfonic acid, was confirmed by synthesis according to the following scheme.
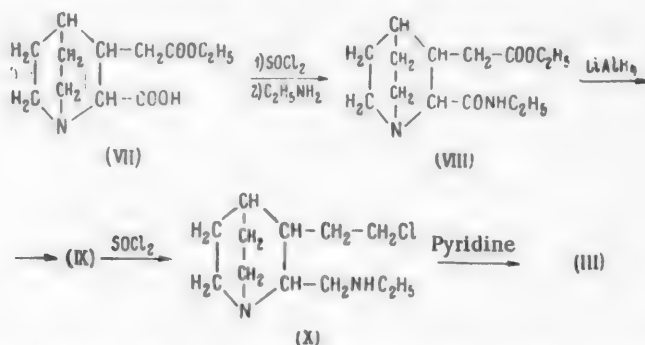
By means of thionyl chloride, the hydrochloride of 3-carbethoxymethyl-quinuclidine-2-carboxylic acid (VII) was converted into the acid chloride, which was reacted with ethylamine to give the ethylamide of this acid (VIII). The amide (VIII) was reduced with lithium aluminum hydride to 2-ethylaminomethyl-3-(β-hydroxyethyl)-quinuclidine (IX). This compound was reacted with thionyl chloride to give 2-ethylaminomethyl-3-(β-chloroethyl)-quinuclidine (X). Heating the latter with piperidine led to 2,3-(3',4'-N-ethylpiperidino)-quinuclidine (III). The substance obtained was identical with the 2,3-(3',4'-N-ethylpiperidino)-quinuclidine isolated in the distillation of the esters (I), (IV) and (V) and also from heating compounds (VI) and (IX) with phthalic anhydride in the presence of benzenesulfonic acid.

Thus, it was established that in the distillation of esters of 2-diethyl(ethyl)aminomethyl-3-(β-hydroxyethyl)-quinuclidine, the tricyclic compound (III) was formed predominantly with the simultaneous liberation of a molecule of an ester or an acid from the acyl group esterifying the original alcohol and the alkyl group or hydrogen at the aminomethyl group in position 2 of the quinuclidine nucleus. Due to this, the synthesis of N-substituted 2-aminomethyl-3-vinylquinuclidines should start from compounds in which the nitrogen atom of the amino-

methyl group in its turn forms part of a cyclic system, which is not cleaved at high temperature. Actually, distillation of 2-(N-piperidinomethyl)-3-(β-steraryloxyethyl)-quinuclidine (XII) at atmospheric pressure gave 2-(N-piperidinomethyl)-3-vinylquinuclidine (XIII) as the sole reaction product. Since the various modes of conversion of 3-(β-hydroxyethyl)-quinuclidine into 3-vinylquinuclidine led mainly to the formation of 3-vinylidenequinuclidine [5], compound (XIII) was oxidized with potassium permanganate to determine the position of the double bond in it. The formation of 2-(N-piperidinomethyl)-quinuclidine-3-carboxylic acid (XIV) in this way indicates the presence of a vinyl group in compound (XIII).

The formation of 2-(N-piperidinomethyl)-3-vinylquinuclidine and its conversions may be represented by the following scheme:

$$
\begin{array}{c}
\text{(XI)} \quad \ce{H2C\overset{CH}{\underset{CH2}{}}CH-CH2-CH2OH \quad CH-CH2-N<CH2-CH2><CH2-CH2>CH2} \\[2mm]
\longrightarrow \quad \text{(XII)} \quad \ce{H2C\overset{CH}{\underset{CH2}{}}CH-CH2-CH2OCOC17H35 \quad CH-CH2-N<CH2-CH2><CH2-CH2>CH2} \longrightarrow \\[4mm]
\text{(XIII)} \quad \ce{H2C\overset{CH}{\underset{CH2}{}}CH-CH=CH2 \quad CH-CH2-N<CH2-CH2><CH2-CH2>CH2} \\[2mm]
\longrightarrow \quad \text{(XIV)} \quad \ce{H2C\overset{CH}{\underset{CH2}{}}CH-COOH \quad CH-CH2-N<CH2-CH2><CH2-CH2>CH2}
\end{array}
$$
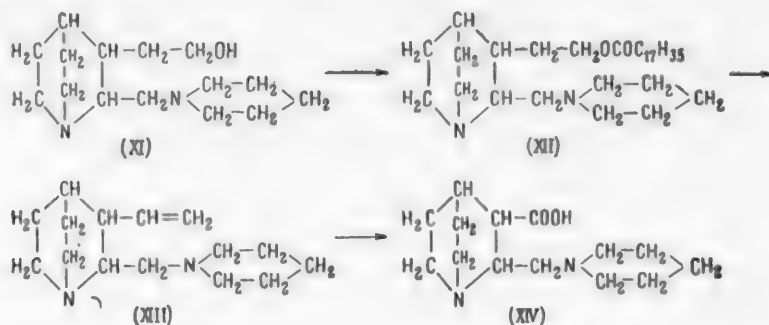
In a previous communication [2], we showed that when the ethyl ester of 3-carbethoxymethylquinuclidine-2-carboxylic acid (XV) was hydrolyzed with water, the substance was only partially hydrolyzed. The acid ester thus formed was ascribed the structure of 3-carbethoxymethylquinuclidine-2-carboxylic acid (VII).

$$
\text{(XV)} \quad \ce{H2C\overset{CH}{\underset{CH2}{}}CH-CH2-COOC2H5 \quad CH-COOC2H5} \longrightarrow \text{(VII)}
$$
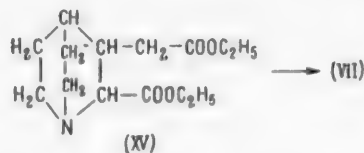
Investigations reported in the present work confirmed the previous proposals. It was noted above that distillation of 2-(N-piperidinomethyl)-3-(β-stearyloxyethyl)-quinuclidine (XII), obtained from the diester (XV) via the acid ester (VII), yielded 2-(N-piperidinomethyl)-3-vinylquinuclidine (XIII), which was converted by oxidation into 2-(N-piperidinomethyl)-quinuclidine-3-carboxylic acid (XIV). Had the hydrolysis of (XV) given the ethyl ester of 3-carboxymethylquinuclidine-2-carboxylic acid (XVI), the vinyl derivative would have had the structure (XVII).

$$
\text{(XV)} \longrightarrow \text{(XVI)} \quad \ce{H2C\overset{CH}{\underset{CH2}{}}CH-CH2-COOH \quad CH-COOC2H5} \longrightarrow \text{(XVII)} \quad \ce{H2C\overset{CH}{\underset{CH2}{}}CH-CH2CH2N<CH2-CH2><CH2-CH2>CH2 \quad C=CH2}
$$
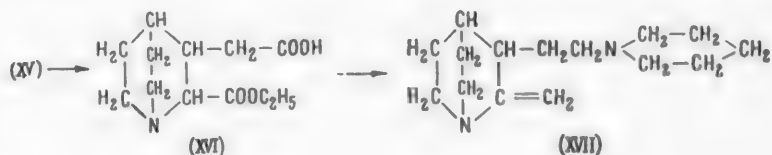
and its oxidation would have led to the corresponding lactam (XVIII),

$$
\text{(XVIII)} \quad \ce{H2C\overset{CH}{\underset{CH2}{}}CH-CH2-CH2-N<CH2-CH2><CH2-CH2>CH2 \quad C=O}
$$
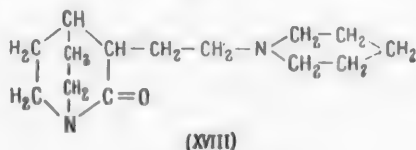
which was not detected among the oxidation products of XIII.

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2-Diethylaminomethyl-3-(β-stearyloxyethyl)-quinuclidine (I). 2.78 g of stearyl chloride was added with stirring to a solution of 2 g of 2-diethylaminomethyl-3-(β-hydroxyethyl)-quinuclidine [2] in 20 ml of benzene. The reaction mixture was boiled for 3 hours, then the solvent removed in vacuum and the residue treated with a 25% solution of potassium carbonate. Th oil liberated was extracted with ether and the ether extract dried with sodium sulfate. Removal of the ether in vacuum yielded 4.15 g (98%) of 2-diethylamino-methyl-3-(β-stearyloxyethyl)-quinuclidine (I) as a soap-like, uncrystallizable mass, which was soluble in organic solvents, but insoluble in water.

The methiodide formed colorless crystals, which were soluble in water and alcohol but insoluble in ether. M. p. 127-128° (from alcohol.

Found %: I 20.04, 20.13. $C_{33}H_{65}O_2N_2I$. Calculated %: I 19.70.

Decomposition of 2-diethylaminomethyl-3-(β-stearyloxyethyl)-quinuclidine. 7 g of 2-diethylamino-methyl-3-(β-stearyloxyethyl)-quinuclidine was heated in a Wurtz flask at 330-360° on a metal bath. The distillation product, 6.4 g of a soap-like mass, was dissolved in ether and the ether solution shaken with 10% hydrochloric acid to separate the base from the neutral substances, dried with potassium carbonate and the solvent removed in vacuum to give 4 g (93%) of ethyl stearate. The m. p. was 34°. The hydrochloric acid extract was made alkaline with 50% potassium carbonate solution and the base extracted with ether. The ether solution was dried with baked potassium carbonate, the ether removed and the residue vacuum distilled. We obtained 1.9 g (71.5%) of a mobile, colorless oil, which gave a positive reaction for a double bond. The b.p. was 94° (0.35 mm).

To separate the unsaturated compound from the saturated substance, 1 g of the mixture obtained was dissolved in 6 g of 10% sulfuric acid and the sulfuric acid solution poured into 14 g of a 10% solution of mercuric acetate in 5% acetic acid. The reaction mixture was heated for 4 hours at 40-50° and cooled, 10 ml of a 29% ammonia solution added (alkaline reaction to phenolphthalein) and the mixture extracted several times with ether. The ether solution was dried with potassium carbonate, the solvent removed and the residue vacuum distilled. We obtained 0.8 g (56.8%) of 2,3-(3',4'- ethylpiperidino)-quinuclidine (III) as a colorless, mobile liquid, which was soluble in organic solvents and water; the b.p. was 84° (0.2 mm), n_D^{26} 1.5035.

Found %: N 14.23, 14.65. $C_{12}H_{22}N_2$. Calculated %: N 14.42.

Picrate. The yellow crystals were soluble in water, acetone and alcohol and insoluble in ether. The m.p. was 238°.

Found %: C 44.40, 44.27; H 4.40, 4.47; N 17.59. $C_{12}H_{22}N_2 \cdot 2C_6H_3O_7N_3$. Calculated %: C 44.30; H 4.30; N 17.20.

Dimethiodide. The colorless crystals were soluble in water and alcohol and insoluble in acetone and ether. The m. p. was 175° (decomp.).

Found %: N 5.90, 5.62. $C_{14}H_{28}N_2I_2$. Calculated %: N 5.86.

After separation of the 2,3-(3',4'-N-ethylpiperidino)-quinuclidine, the ammoniacal mother solution contained the addition product of mercuric acetate and 2-diethylaminomethyl-3-vinylquinuclidine. To decompose this product, the ammoniacal solution was acidified with 20 ml of 20% sulfuric acid. To the sulfuric acid solution was added 0.5 g of phosphorous acid and the mixture boiled for 7 minutes. The mercury formed was filtered off and the filtrate treated with 50% potassium carbonate solution and extracted with ether. The ether extracts were dried with potassium carbonate, the ether removed and the residue distilled. We obtained 0.05 g (3.5%) of 2-diethylaminomethyl-3-vinylquinuclidine (II); b. p. 100° (3 mm), $n_D^{16.3}$ 1.4995.

Found %: N 12.8, 12.94. $C_{14}H_{26}N_2$. Calculated %: N 12.62.

2-Diethylaminomethyl-3-(β-benzoyloxyethyl)-quinuclidine (IV). 0.64 g of benzoyl chloride was added to a solution of 1 g of 2-diethylaminomethyl-3-(β-hydroxyethyl)-quinuclidine in 10 ml of anhydrous benzene and the mixture boiled for 3 hours. The reaction mixture was cooled to room temperature and extracted three

times the 10 ml of 10% hydrochloric acid. The hydrochloric acid extracts were combined, washed with ether, treated with 50% potassium carbonate solution and extracted with chloroform. The chloroform solution was dried with potassium carbonate, the solvent removed in vacuum and the residue distilled. We obtained 1.2 g (84%) of 2-diethylaminomethyl-3-(β-benzoyloxyethyl)-quinuclidine (IV) as an immobile yellow oil, which was readily soluble in organic solvents but insoluble in water; b. p. 175° (0.25 mm), $n^{22}D$ 1.5216.

Found %: C 72.20, 71.8; H 9.55, 9.51; N 8.33, 8.12. $C_{21}H_{32}O_2N_2$. Calculated %: C 72.20; H 9.30; C 72.20; H 9.30; N 8.11.

Decomposition of 2-diethylaminomethyl-3-(β-benzoyloxyethyl)-quinuclidine. 3.55 g of 2-diethylamino-methyl-3-(β-benzoyloxyethyl)-quinuclidine was heated on a metal bath at 315°. We obtained 3.2 g of distillate. To separate the neutral substances, the distillate was dissolved in 10% hydrochloric acid and the hydrochloric acid solution extracted with ether. The ether extract was dried with potassium carbonate. After removal of the solvent, the residue was distilled. We obtained 1.22 g (79%) of the ethyl benzoate: b. p. 212°, $n^{15}D$ 1.507.

Found %: C 72.03, 71.81; H 6.98, 6.58. $C_9H_{10}O_2$. Calculated %: C 72; H 6.66.

The hydrochloric acid solution was treated with 50% potassium carbonate solution and the reaction product extracted with ether. The ether solution was dried with potassium carbonate, the solvent removed in vacuum and the residue distilled. We obtained 1.35 g (67.5%) of 2,3-(3',4'-N-ethylpiperidino)-quinuclidine; b. p. 84° (0.2 mm) $n^{16}D$ 1.5091.

Found %: N 14.19, 13.97. $C_{12}H_{22}N_2$. Calculated %: N 14.42.

The picrate had m. p. 239°

Found %: C 44.15, 44.81; H 4.44, 4.46; N 17.59, 17.42. $C_{12}H_{22}N_2 \cdot 2C_6H_3O_7N_3$. Calculated %: C 44.30; H 4.30; N 17.20.

Ethylamide of 3-carbethoxymethyl-quinuclidine-2-carboxylic acid (VIII). 7.83 g of the hydrochloride of 3-carbethoxymethyl-quinuclidine-2-carboxylic acid [2] and 80 ml of thionyl chloride were heated for 4 hours at 65-70°. The excess thionyl chloride was removed in vacuum, with the last traces removed by adding benzene twice and distilling it off. The hydrochloride of the acid chloride of 3-carbethoxymethyl-quinuclidine-2-carboxylic acid thus obtained was treated with 100 ml of a 34% solution of ethylamine in dry ether with cooling. The reaction mixture was allowed to stand for 1 hour, then 30 ml of 50% potassium carbonate solution was added and the amide extracted with chloroform. The chloroform solution was dried with potassium carbonate. the solvent removed and the residue vacuum distilled. We obtained 6.41 g (85%) of the ethylamide of 3-carb-ethoxy-1-quinuclidine-2-carboxylic acid (VIII) as an immobile yellow oil, which was soluble in organic solvents and water; b. p. 159-160° (0.6 mm), $n^{18}D$ 1.4949.

Found %: C 62.52, 62.19; H 8.76, 8.87; N 10.18. $C_{14}H_{24}O_3N_2$. Calculated %: C 62.69; H 8.95; N 10.45.

2-Ethylaminomethyl-3-(β-hydroxyethyl)-quinuclidine (IX). A solution of 6 g of the ethylamide of 3-carbethoxymethyl-quinuclidine-2-carboxylic acid in 60 ml of benzene was added with stirring to a suspension of 3.4 g of lithium aluminum hydride in 60 ml of ether. The reaction mixture was boiled for 20 hours. Then 6.5 ml of water was added with stirring and cooling and the lithium and aluminum hydroxides filtered off and washed with chloroform. The combined extracts were dried with potassium carbonate, the solvent removed and the residue vacuum distilled. We obtained 3.8 g (85%) of 2-ethylaminomethyl-3-(β-hydroxyethyl)-quinucli-dine (IX) as a colorless mobile liquid, which was readily soluble in organic solvents and water. The b. p. was 134° (0.7 mm).

Found %: N 13.17, 13.15. $C_{12}H_{24}ON_2$. Calculated %: N 13.20.

2-Ethylaminomethyl-3-(β-benzoyloxyethyl)-quinuclidine (V). A solution of 1.7 g of 2-ethylamino-methyl-3-(β-hydroxyethyl)-quinuclidine and 0.98 g of benzoic acid in 20 ml of dry benzene was saturated with hydrogen chloride. The reaction mixture was then boiled for 5 hours. The benzene was removed in vacuum, the residue treated with 50% potassium carbonate solution and the liberated oil extracted with ether. The ether solution was dried with potassium carbonate. After removal of the ether, the residue was vacuum distilled. We obtained 1.75 g (69%) of 2-ethylaminomethyl-3-(β-benzoyloxyethyl)-quinuclidine (V). The

immobile, greenish liquid was soluble in organic solvents but insoluble in water. The b.p. was 160° (0.3 mm).

Found %: C 72.4; H 8.7. $C_{19}H_{29}O_2N_2$. Calculated %: C 72.15; H 8.85.

Decomposition of 2-ethylaminomethyl-3-(β-benzoyloxyethyl)-quinuclidine. 0.7 g of 2-ethylaminomethyl-3-(β-benzoyloxyethyl)-quinuclidine was heated on a metal bath at 360°. The liquid distilling off (0.35 g) was collected and dissolved in 10% hydrochloric acid. The hydrochloric acid solution was extracted with ether and the ether evaporated to give 0.1 g (34.5%) of benzoic acid. The m.p. was 119°. The hydrochloric acid mother solution was treated with 50% potassium carbonate solution and extracted with ether. The ether solution was dried over potassium carbonate. After removal of the solvent, the residue was vacuum distilled. We obtained 0.2 g (43.5%) of 2,3-(3',4'-N-ethylpiperidino)-quinuclidine (III); $n^{17}D$ 1.5101, and b. p. 82° (0.2 mm). The picrate melted at 238°.

Reaction of 2-diethylaminomethyl-3-(β-hydroxyethyl)-quinuclidine with phthalic anhydride in the presence of benzenesulfonic acid. A mixture of 2 g of 2-diethylaminomethyl-3-(β-hydroxyethyl)-quinuclidine, 8.65 g of phthalic anhydride and 3.32 g of benzenesulfonic acid was heated at 280-285° for 15 minutes. 33% sodium hydroxide solution was added to the reaction mixture until it was alkaline to phenolphthalein and then it was steam distilled. The distillate was acidified with concentrated hydrochloric acid and evaporated to small volume on a steam bath. The residue was treated with 50% potassium carbonate solution and the reaction product extracted with ether. When the ether extract had been dried with potassium carbonate and the solvent removed, the residue was vacuum distilled. We obtained 0.8 g (49.5%) of 2,3-(3',4'-N-ethylpiperidino)-quinuclidine; b. p. 95° (0.35 mm), $n^{17}D$ 1.5087. The picrate melted at 237°.

Reaction of 2-ethylaminomethyl-3-(β-hydroxyethyl)-quinuclidine with phthalic anhydride in the presence of benzenesulfonic acid. 1 g of 2-ethylaminomethyl-3-(β-hydroxyethyl)-quinuclidine, 4.35 g of phthalic anhydride and 1.68 g of benzenesulfonic acid were heated at 280° for 15 minutes. Working up as in the previous experiment yielded 0.35 g (38.4%) of 2,3-(3',4'-N-ethylpiperidino)-quinuclidine; b. p. 87° (0.3 mm), $n^{17}D$ 1.5085. The picrate melted at 238°.

2,3-(3',4'-N-Ethylpiperidino)-quinuclidine (III). An alcohol solution of hydrogen chloride was added to 30 g of 2-ethylaminomethyl-3-(β-hydroxyethyl)-quinuclidine (IX) until it was acid to Congo. The alcohol was removed in vacuum and the residue dissolved in 30 ml of anhydrous chloroform. 120 ml of thionyl chloride was added to the chloroform solution of the amino alcohol hydrochloride (IX) obtained and the reaction mixture boiled for 4 hours. The chloroform and excess thionyl chloride were removed in vacuum, the residue treated with 50% potassium carbonate solution and the liberated 2-ethylaminomethyl-3-(β-chloroethyl)-quinuclidine (X) extracted with ether. The ether solution was dried with sodium sulfate, the ether removed and the product (X) boiled with 300 ml of pyridine for 2 hours. After removal of the pyridine in vacuum, the residue was treated with 300 ml of 50% potassium carbonate and the reaction product extracted with ether. The ether extract was dried with potassium carbonate, the ether removed and the residue vacuum distilled. We obtained 10.5 g (38.5%) of 2,3-(3',4'-N-ethylpiperidino)-quinuclidine (III); b. p. 82° (0.2 mm), $n^{17}D$ 1.5100.

Found %: N 14.68, 14.35. $C_{12}H_{22}N_2$. Calculated %: N 14.42.

The picrate had m. p. 238-239°.

Found %: C 43.70, 43.88; H 4.10, 4.50; N 17.53. $C_{12}H_{22}N_2 \cdot 2C_6H_3O_7N_3$. Calculated %: C 44.3; H 4.30; N 17.20.

The dimethiodide had m.p. 175° (decomp.).

Found %: N 5.8, 5.42. $C_{14}H_{28}N_2I_2$. Calculated %: N 5.86.

The 2,3-(3',4'-N-ethylpiperidino)-quinuclidine obtained was identical (mixed melting points of picrate and methiodides) with the compound isolated in the decomposition of the esters (I), (IV) and (V) and from heating the hydroxyamines (VI) and (IX) with phthalic anhydride in the presence of benzenesulfonic acid.

2-(N-Piperidinomethyl)-3-(β-stearyloxyethyl)-quinuclidine (XII). A solution of 2 g of 2-(N-piperidinomethyl)-3-(β-hydroxyethyl)-quinuclidine [2] and 2.7 g of stearyl chloride in 20 ml of anhydrous chloroform was boiled for 4 hours. The cooled solution deposited crystals on standing for a day and these were filtered off and washed with alcohol. We obtained 3.5 g (75%) of the dihydrochloride of 2-(N-piperidinomethyl)-3-(β-stearyloxyethyl)-quinuclidine. The colorless crystals were insoluble in water and ether and sparingly soluble in alcohol. The m. p. was 180-182° (from alcohol).

Found %: Cl 11.82, 11.97; N 4.62, 4.23. $C_{33}H_{64}O_2N_2Cl_2$. Calculated %: Cl 11.84; N 4.74.

Decomposition of 2-(N-piperidinomethyl)-3-(β-staryloxyethyl)-quinuclidine. 1.5 g of 2-(N-piperidino-methyl)-3-(β-staryloxyethyl)-quinuclidine was boiled for 2 minutes. The reaction product was distilled off at atmospheric pressure and dissolved in 10% hydrochloric acid and the hydrochloric acid solution extracted with ether to remove the acid-insoluble substances. The hydrochloric acid solution was made alkaline with 50% potassium carbonate solution and extracted with ether. The ether extract was dried with potassium carbonate, the ether removed and the residue vacuum distilled. We obtained 0.2 g of 2-(N-piperidinomethyl)-3-vinylquinuclidine as a mobile, colorless oil, which was soluble in water and organic solvents. The substance contained a double bond (test with potassium permanganate). The b. p. was 123-125° (0.25 mm).

Found %: C 76.57, 77.33; H 10.88, 10.88; N 11.68, 12.03. $C_{15}H_{26}N_2$. Calculated %: C 76.92; H 11.12; N 11.96.

The ether extract was evaporated to give 0.4 g of stearic acid. The m.p. was 69°.

Oxidation of 2-(N-piperidinomethyl)-3-vinylquinuclidine. A solution of 3.78 g of potassium perman-ganate in 100 ml of water was added over a period of 3 hours to a solution of 2.6 g of 2-(N-piperidinomethyl)-3-vinylquinuclidine in 21 ml of 10% sulfuric acid at 0-5°. During the oxidation, a slightly acid reaction was maintained by the periodic addition of 10% sulfuric acid. When the oxidation was complete, the manganese di-oxide was filtered off and washed with hot water. The aqueous filtrate was evaporated to small volume, the residue treated with 50% potassium carbonate solution and the unreacted material extracted with chloroform. The alkaline solution was acidified with concentrated hydrochloric acid and evaporated to dryness. The dry residue was boiled with 30 ml of 11% hydrogen chloride in alcohol for 4 hours. Then the alcohol was distilled off in vacuum and the residue again heated with an alcohol solution of hydrogen chloride. After removal of the alcohol, the reaction mixture was dissolved in a small amount of water, 50% potassium carbonate solution added to the aqueous solution, which was the extracted with ether. The ether solution was dried with potassium carbonate. After removal of the solvent, the substance was vacuum distilled. We obtained 0.5 g of the ethyl ester of 2-(N-piperidinomethyl)-quinuclidine-3-carboxylic acid; b. p. 144° (0.25 mm), $n^{14}D$ 1.4982.

Found %: N 9.69, 9.34. $C_{16}H_{28}O_2N_2$. Calculated %: N 10.00.

Hydrochloride of 2-(N-piperidinomethyl)-quinuclidine-3-carboxylic acid (XIV). 0.2 g of the ethyl ester of 2-(N-piperidinomethyl)-quinuclidine-3-carboxylic acid and 3 ml of concentrated hydrochloric acid were boiled for 4 hours. The reaction mixture was evaporated in vacuum, the residue triturated with ether and the crystals produced filtered off. We obtained 0.1 g of the hydrochloride of 2-(N-piperidinomethyl)-quinuclidine-3-carboxylic acid as colorless hygroscopic crystals, which were soluble in water and alcohol. The m. p. 232°.

Found %: C 48.65; H 7.9; Cl 20.54. $C_{14}H_{25}O_2N_2Cl \cdot H_2O$. Calculated %: C 48.97; H 8.16; Cl 20.63.

Hydrazide of 2-(N-piperidinomethyl)-quinuclidine-3-carboxylic acid. A solution of 0.1 g of the ethyl ester of 2-(N-piperidinomethyl)-quinuclidine-3-carboxylic acid and 1 ml of hydrazine hydrate in 2 ml of alcohol was boiled for 4 hours. The alcohol and excess hydrazine hydrate were removed in vacuum. The resi-due, which formed an uncrystallizable mass, was dissolved in alcohol and a solution of picric acid added to the alcohol solution. We obtained 0.1 g of the tripicrate of the hydrazide as yellow crystals, which were solu-ble in acetone and water, sparingly soluble in alcohol and insoluble in ether. The m. p. was 100°.

Found %: C 39.89; H 3.96; N 19.20. $C_{32}H_{35}O_{22}N_{13}$. Calculated %: C 40.29; H 3.67; N 19.09.

SUMMARY

1. It was found that distillation of the esters of 2-diethyl(ethyl)aminomethyl-3-(β-hydroxyethyl)-quinucli-dines and also heating 2-diethyl(ethyl)aminomethyl-3-(β-hydroxyethyl)-quinuclidine with phthalic anhydride gave 2,3-(3',4'-N-ethylpiperidino)-quinuclidine.

2. Distillation of 2-(N-piperidinomethyl)-3-(β-staryloxyethyl)-quinuclidine at atmospheric pressure yielded 2-(N-piperidinomethyl)-3-vinylquinuclidine.

3. The structure of 2,3-(3',4'-N-ethylpiperidino)-quinuclidine was confirmed by synthesis, starting from 3-carbethoxymethylquinuclidine-2-carboxylic acid.

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*Original Russian pagination. See C.B. Translation.

HOFMANN DEGRADATION OF 1-AZABICYCLO-(3,2,1)-OCTANE

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In the Hofmann degradation of symmetrical bicyclic systems with a common nitrogen, the theoretically possible result is the formation of one monocyclic heterocycle with a methylated nitrogen and an unsaturated side chain or the products of its conversion [1, 2] and an unsaturated monocycle, methylated at the nitrogen [1].

On the other hand, in the degradation of unsymmetrical bicyclic systems with a common nitrogen, there is the possibility of the formation of three monocycles with an unsaturated side chain or the products of their conversion, depending on which β-carbon atom will lose a hydrogen for the formation of a molecule of water. The direction of cleavage will apparently depend both on the comparative stability of the bicycles and on the experimental conditions. We confirmed this hypothesis by studying the cleavage of 1-azabicyclo-(3,2,1)-octane (III). The 1-azabicyclo-(3,2,1)-octane required for the work was synthesized starting from 1-carbethoxy-methyl-3-carbethoxypiperidine (I) [3] by the following scheme.
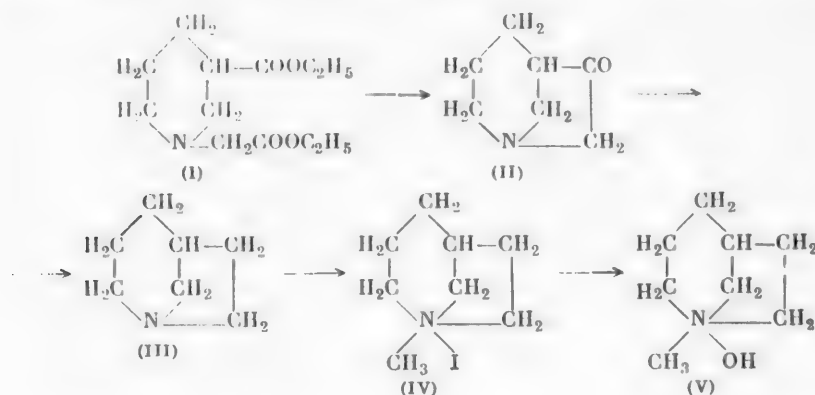
The intramolecular condensation of the diester (I) into 1-azabicyclo-(3,2,1)-octanone-6-(II) was accomplished in the presence of potassium alcoholate instead of metallic potassium, as directed in the literature [3] and this made it possible to increase the yield of the ketone (II) from 30-36 to 71%. Reduction of the ketone (II) by Kizhner's method [4] gave 1-azabicyclo-(3,2,1)-octane (III), which reacted with methyl iodide to form the quaternary salt (IV) and treating this with silver oxide gave the corresponding quaternary base (V).

We studied the cleavage of 1-azabicyclo-(3,2,1)-octane under various conditions: heating the quaternary base (V) at atmospheric pressure, in vacuum at 50-55 mm and in sealed tubes and also heating the methiodide (IV) in the presence of 40% potassium hydroxide solution. When the quaternary base of 1-azabicyclo-(3,2,1)-octane (V) was heated to 250° at atmospheric pressure, two substances were isolated — an unsaturated compound in 39% yield and a substance, which did not contain a double bond, in 20% yield.

According to elementary analysis data, the unsaturated compound obtained had the composition $C_8H_{15}N$, which corresponds to the composition of one of the possible decomposition products of substance (V).

(V)

CH₂
H₂C   CH—CH=CH₂
H₂C   CH₂
      N
      CH₃
      (A)

CH₂   CH₂
H₂C   CH—CH₂
H₂C
      N——CH₂
      CH₃
      (B)

CH₂=CH—CH₂—HC——CH₂
              H₂C   CH₂
                 N
                 CH₃
                (VI)
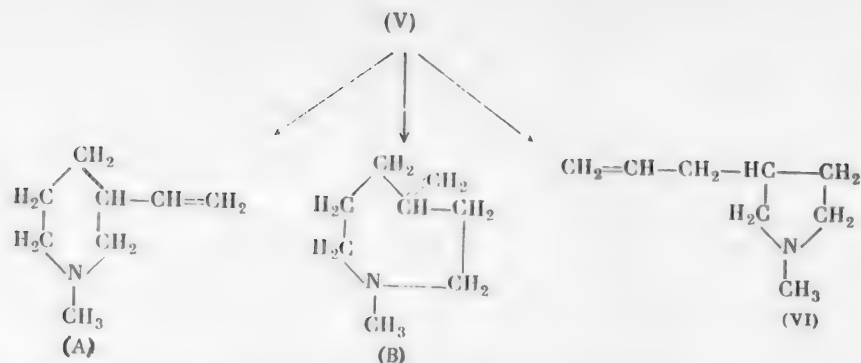
When the unsaturated compound was oxidized with potassium permanganate, we obtained a substance containing a carboxyl group, which excludes the structure of the seven-membered ring (B), whose oxidation would lead to a ketone.

Reduction of the unsaturated degradation product led to a substance, identical with 1-methyl-3-propyl-pyrrolidine (X), which we prepared, starting from 1,4-dibromo-3-propylbutane (XV) [5], by heating the latter with an aqueous solution of methylamine in a sealed tube. Consequently, the unsaturated compound, formed by degradation of the quaternary base of 1-azabicyclo-(3,2,1)-octane, was 1-methyl-3-allylpyrrolidine (VI) and the acid obtained by oxidizing it had the structure of 1-methylpyrrolidyl-3-acetic acid (XII).

The second substance, isolated as a result of degrading the quaternary base (V) by heating at atmospheric pressure, had the composition $C_{16}H_{32}ON_2$ according to analysis and molecular weight data. Heating the latter with 67% hydrobromic acid in a sealed tube [6] gave a bromide hydrobromide with the composition $C_8H_{17}NBr_2$. This conversion indicated that the substance with composition $C_{16}H_{32}ON_2$ was an ether. The bromide hydro-bromide (VIII) was reduced with zinc dust in hydriodic acid [7]. The reduction product was identical with 1-methyl-3-ethylpiperidine (XIII), which we synthesized starting from 3-acetylpiperidine (XVI) [8]. Consequently, the bromide was 1-methyl-3-(β-bromoethyl)-piperidine (VIII) and the substance with the composition $C_{16}H_{32}ON_2$ was di-[β-(1-methylpiperidyl-3)]-ethyl ether (VII).

When treated with an alcohol solution of potassium hydroxide, the bromide hydrobromide (VIII) gave an internal salt, which we isolated as the methchloride of 1-azabicyclo-(3,2,1)-octane (XIV). Treatment of the latter with silver oxide gave a quaternary base, which was acidified with hydriodic acid to give a substance identical with the original methiodide of 1-azabicyclo-(3,2,1)-octane (IV).

Degradation of the quaternary base (V) in vacuum yielded 1-methyl-3-allylpyrrolidine (VI) in 52% yield and 6% of a mixture, from which it was impossible to isolate individual substances. When the methiodide of 1-azabicyclo-(3,2,1)-octane was heated with 40% potassium hydroxide solution, we isolated 1-methyl-3-allyl-pyrrolidine (VI) (65%) and di-[β-(1-methylpiperidyl-3)]-ethyl ether (VII) (5%).

Heating (V) in water in a tube at 200° led to small amounts of 1-methyl-3-allylpyrrolidine (VI) and di[β-(1-methylpiperidyl-3)]-ethyl ether (VII) and a 35% yield of a new substance with the composition $C_8H_{17}NO$, which did not contain a double bond. When this compound was treated with 67% hydrobromic acid in a sealed tube at 100-110° in a bath [6], it formed a bromide hydrobromide, which was identical with the hydrobromide of 1-methyl-3-(β-bromoethyl)-piperidine (VIII), described above. Consequently, the substance with composition $C_8H_{17}ON$ was 1-methyl-3-(β-hydroxyethyl)-piperidine (IX).

The material given below on the Hofmann degradation of 1-azabicyclo-(3,2,1)-octane may be represented by the scheme presented.

The data obtained indicate that degradation of the quaternary base of 1-azabicyclo-(3,2,1)-octane un-der various condition always produces 1-methyl-3-allylpyrrolidine. This compound is the main degradation product when the quaternary salt (IV) of the quaternary base (V) is heated in vacuum and with 40% potassium hydroxide. Degradation of (V) at atmospheric pressure yields di-[β-(1-methylpiperidyl-3)]-ethyl ether besides

1-methyl-3-allylpyrrolidine and heating (V) under pressure gives 1-methyl-3-(β-hydroxyethyl)-piperidine as well as the two substances named.

EXPERIMENTAL

1-Azabicyclo-(3,2,1)-octanone-6 (II). A solution of 54 ml (42.43 g) of anhydrous alcohol in 50 ml of toluene was gradually added with stirring to a suspension of 36 g of metallic potassium in 100 ml of anhydrous toluene. The reaction mixture was boiled for 2 hours. A solution of 90 g of 1-carbethoxymethyl-3-carbethoxy-piperidine (I) in 240 ml of anhydrous toluene was added to the potassium alcoholate formed over a period of 1 hour, while the mixture was kept boiling evenly. When the diester (I) had been added, the reaction mixture was boiled for 5 hours. The toluene solution gradually deposited a brownish red precipitate of the potassium salt of 1-azabicyclo-(3,2,1)-octanone-6. 400 ml of concentrated hydrochloric acid was carefully added to the cooled reaction mixture with stirring and cooling, the toluene layer was separated

and washed with 400 ml of hydrochloric acid and the combined hydrochloric acid solutions boiled . for 15 hours The hydrochloric acid solution was then decolorized with activated charcoal and evaporated on a steam bath. The cooled residue was treated with excess 50% potassium hydroxide solution. The potassium chloride was filtered off and washed with a small amount of ice water and ether and the mother solution carefully extracted with ether. The ether solution was dried with potassium carbonate and the ether removed in vacuum. We obtained 33 g (71%) of 1-azabicyclo-(3,2,1)-octanone-6 (II). The white, hygroscopic needle-like crystals had m.p. 129-130° (from petroleum ether).

The hydrochloride formed white prisms with m.p. 270° [4].

1-Azabicyclo-(3,2,1)-octane (III). 8.5 g of 1-azabicyclo-(3,2,1)-octanone-6 (II), 12.75 g of pure potassium hydroxide, 8.5 ml of hydrazine hydrate and 85 ml of anhydrous glycerol were slowly (frothing is possible) heated to 165-170° (in the bath) and kept at this temperature for 5 hours. Then the 1-azabicyclo-(3,2,1)-octane (III) was steam distilled from the reaction mixture while the temperature was gradually raised to 250°. The distillate was extracted with ether, the ether extract dried with sodium sulfate, the ether evaporated and the residue distilled. The yield was 7 g (92%). The b. p. was 150-153°. The colorless oil with a sharp amine smell was readily soluble in organic solvents and water. When cooled it solidified to clear hygroscopic crystals with m. p. 84°.

The methiodide formed white crystals which were readily soluble in water, sparingly so in alcohol and acetone and insoluble in ether. The m. p. was 340-342° (decomp.) (from acetone).

Found %: N 5.51. $C_8H_{16}NI$. Calculated %: N 5.53.

Hofmann degradation of 1-azabicyclo-(3,2,1)-octane at atmospheric pressure. A solution of 30 g of the methiodide of 1-azabicyclo-(3,2,1)-octane (IV) in 100 ml of distilled water was shaken for 5 hours with moist silver oxide prepared from 40 g of silver nitrate. The silver iodide and excess silver oxide were filtered off, washed well with distilled water and the combined mother solution evaporated in vacuum. The residual oil, which was the quaternary base, was transferred to a Wurtz flask and heated on a bath to 200° at atmospheric pressure. Even at 130° (in the bath) the reaction mixture frothed and a distillate began to come over. A fraction was collected which boiled in the range 100-170°. To separate the oily from the aqueous layer, the distillate was extracted with ether, the ether extract dried with potassium carbonate, the ether removed and the residue distilled at atmospheric pressure. The b. p. was 149-152°. We obtained 5.7 g (39.3%) of 1-methyl-3-allylpyrrolidine (VI) as a colorless mobile liquid, which was readily soluble in organic solvents, but sparingly so in water and had a sharp amine smell and $n^{20}D$ 1.4462.

Found %: C 76.47; H 12.19; N 11.19. $C_8H_{15}N$. Calculated %: C 76.80; H 12.00; N 11.20.

The picrate formed yellow crystals with m. p. 118-120° (from alcohol).

Found %: C 47.62; H 5.24; N 15.77. $C_{14}H_{18}O_7N_4$. Calculated %: C 47.5; H 5.08; N 15.82.

The methiodide formed white crystals with m. p. 136-138° (from acetone).

Found %: N 5.20. $C_9H_{18}NI$. Calculated %: N 5.25.

When the 1-methyl-3-allylpyrrolidine had been distilled off, the Wurtz flask contained a high-boiling residue. The latter was dissolved in ether, the ether solution dried with potassium carbonate, the ether removed and the substance vacuum distilled. We obtained 2.9 g (20.7%) of di[β-(1-methylpiperidyl -3)]-ethyl ether (VII) as a colorless oil, which was soluble in organic solvents but sparingly so in water. The b. p. was 154-155°, (5 mm) and the $n^{20}D$ 1.4793.

Found %: C 70.83; H 11.93; N 10.41. M 263 (by Rast's method). $C_{16}H_{32}ON_2$. Calculated %: C 71.64; H 11.92; N 10.44, M 265.

The picrate formed yellow crystals with m.p. 178-180° (from alcohol).

Found %: C 46.19; H 5.12; N 15.11. $C_{28}H_{38}O_{15}N_8$. Calculated %: C 46.28; H 5.23; N 15.42.

The methiodide formed white crystals with m. p. 196-197° (from alcohol).

Ethyl ester of 1-methylpyrrolidyl-3-acetic acid (XI). Over a period of 3 hours, 14.5 g of potassium permanganate as a 4% aqueous solution was added with stirring to a solution of 4.3 g of 1-methyl-3-allylpyrrolidine

in 100 ml of water and 62 ml of 10% sulfuric acid, while the temperature of the mixture was kept below 4°. When the oxidant had been added, the reaction mixture was stirred for a further 2 hours at the same temperature. The manganese dioxide was then filtered off and washed carefully with hot water. The combined aqueous solutions were acidified to Congo with sulfuric acid and evaporated in vacuum. The residue, containing the hydrosulfate of 1-methylpyrrolidyl-3-acetic acid (XII) and inorganic salts, was dried by addition and vacuum distillation of anhydrous alcohol. Then the hydrosulfate of the acid was extracted with hot anhydrous alcohol. Distillation of the alcohol yielded 5.65 g of a caramel-like mass, which was heated with a 10-fold amount of a 4% alcohol solution of hydrogen chloride for 3 hours. The alcohol was removed in vacuum and the residue treated with 50% potassium carbonate solution and extracted with ether. When the extract had been dried and the ether removed, the substance was vacuum distilled. We obtained 3 g (51%) of the ethyl ester of 1-methylpyrrolidyl-3-acetic acid (XI) as a colorless, mobile liquid. The b. p. was 88° (9 mm) and n^{20}D 1.4451.

Found %: N 8.10. $C_9H_{17}O_2N$. Calculated %: N 8.18.

1-Methylpyrrolidyl-3-acetic acid (XII). 0.5 g of the ethyl ester of 1-methylpyrrolidyl-3-acetic acid and 5 ml of concentrated hydrochloric acid were boiled for 7 hours. The hydrochloric acid solution was decolorized with activated charcoal and evaporated in vacuum. The residue, which formed a caramel-like mass, crystallized when triturated with dry acetone. The crystals were filtered off, washed with acetone and dried. We obtained 0.36 g (70%) of the hydrochloride of 1-methylpyrrolidyl-3-acetic acid (XII). The white crystalline powder was readily soluble in water and alcohol and insoluble in ether, acetone and chloroform. The m. p. was 94-96° (from a mixture of alcohol and acetone).

Found %: C 46.34; H 7.78; N 7.54; Cl 19.85. $C_7H_{14}O_2NCl$. Calculated %: C 46.79; H 7.8; N 7.8; Cl 19.72.

1-Methyl-3-propylpyrrolidine (X). a) To a solution of 3.3 g of 1-methyl-3-allylpyrrolidine (VI), obtained by degradation of the quaternary base of 1-azabicyclo-(3,2,1)-octane (V), in 50 ml of anhydrous alcohol was added 4 ml of a 20% alcohol solution of hydrogen chloride and 0.15 g of platinum oxide (Adam's catalyst). The reaction mixture was shaken with hydrogen at room temperature. When the required amount of hydrogen had been absorbed (1 mole), the platinum black was filtered off and the alcohol removed in vacuum. The residue was treated with excess 50% potassium carbonate solution and extracted with ether. The ether solution was dried with potassium carbonate, the ether removed and the substance distilled at atmospheric pressure. We obtained 3 g (90%) of 1-methyl-3-propylpyrrolidine (X) as a colorless, volatile oil with a sharp amine smell and which was readily soluble in organic solvents and sparingly so in water. The b. p. was 150-152° and n^{20}D 1.4350.

The methiodide formed white crystals with m. p. 156-157° (from acetone).

The picrate formed yellow crystals with m.p. 134-135° (from alcohol).

Found %: C 47.20; H 5.63; N 15.3. $C_{14}H_{20}O_6N_4$. Calculated %: C 47.19; H 5.62; N 15.73.

b) A mixture of 5 g of 1,4-dibromo-3-propylbutane, prepared by the scheme in [5], and 25 ml of 33% aqueous methylamine solution was heated in a sealed tube for 15 hours at 160-180° (in the bath). The reaction mixture consisted of two layers, the upper one oil and the lower one water. The oil was extracted with ether, the ether solution dried with potassium carbonate, the ether removed and the residue distilled at atmospheric pressure. We obtained 1.5 g (61%) of 1-methyl-3-propylpyrrolidine. The b. p. was 150-152° and n^{20}D 1.4348.

The methiodide formed white crystals with m. p. 156-157° (from acetone). The picrate appeared as yellow crystals with m. p. 134-135° (from alcohol).

The picrate and the methiodide did not depress the melting points of the picrate and the methiodide of 1-methyl-3-propyloyrrolidine, isolated in the reduction of 1-methyl-3-allylpyrrolidine.

The hydrobromide of 1-methyl-3-(β-bromoethyl)-piperidine (VIII). 1.5 g of di-[β-(1-methylpiperidyl-3)]-ethyl ether (VII) and 25 ml of 67% hydrobromic acid were heated in a sealed tube at 100-110° for 6 hours. The reaction mixture was evaporated in vacuum and the residue crystallized from acetone. We obtained 2.5 g (77%) of the hydrobromide of 1-methyl-3-(β-bromethyl)-piperidine (VIII). The substance formed white crystals, which were readily soluble in water, sparingly so in alcohol and acetone and insoluble in ether. The m. p. was 134-136°.

Found %: Br 55.52. $C_9H_{17}NBr_2$. Calculated %: Br. 55.75.

Reaction of the hydrobromide of 1-methyl-3-(β-bromoethyl)-piperidine (VIII) with potassium hydroxide. To a hot solution of 2 g of the hydrobromide of 1-methyl-3-(β-bromoethyl)-piperidine in 5 ml of 94% methyl alcohol was added a hot solution of 1.3 g of potassium hydroxide in 5 ml of 94% methyl alcohol and the mixture boiled for 10 hours. The alcohol solution was then acidified with hydrochloric acid and evaporated on a steam bath. The residue was extracted with anhydrous alcohol and the alcohol removed in vacuum. We obtained 1 g of the methchloride of 1-azabicyclo-(3,2,1)-octane. The substance did not melt up to 350°.

Found %: C 59.15; H 9.89; N 8.56; Cl 21.92. $C_8H_{16}NCl$. Calculated %: C 59.44; H 9.9; N 8.67; Cl 21.92.

0.4 g of the methchloride of 1-azabicyclo-(3,2,1)-octane (XIV), 10 ml of water and 1.08 g Ag_2O were shaken together for 2 hours at room temperature. The silver chloride and excess silver oxide were filtered off, washed thoroughly with distilled water and the combined mother solutions acidified with hydriodic acid and evaporated in vacuum. The residue (0.63 g) was recrystallized from acetone. We obtained 0.35 g of the methiodide of 1-azabicyclo-(3,2,1)-octane as white crystals. The m. p. was 340-342°. The substance did not depress the melting point of the original methiodide of 1-azabicyclo-(3,2,1)-octane (IV).

Found %: N 5.35; I 49.2. $C_8H_{16}NI$. Calculated %: N 5.53; I 50.15.

1-Methyl-3-ethylpiperidine (XIII). a) Over a period of 1 hour, 5 g of zinc dust was added with stirring to a solution of 5 g of the hydrobromide of 1-methyl-3-(β-bromoethyl)-piperidine in 40 ml of hydriodic acid at 5°. The reaction mixture was kept at this temperature for 3 days, while a further 40 ml of hydriodic acid was added gradually. The sludge was filtered off and the mother solution evaporated on a steam bath. The caramel-like residue was treated with excess 50% potassium hydroxide solution and extracted with ether, the ether extract dried with potassium carbonate, the ether removed and the substance distilled at atmospheric pressure. We obtained 0.45 g (20%) of a very volatile, colorless oil with a sharp amine smell. The b. p. was 149-151° and $n^{20}D$ 1.4460.

The methiodide formed white crystals. The m. p. was 191-192° (from acetone).

Found %: N 5.15. $C_9H_{20}NI$. Calculated %: N 5.20.

The picrate formed yellow crystals with m. p. 130-132° (from alcohol).

The picrate and the methiodide did not depress the melting points of the picrate and methiodide of 1-methyl-3-ethylpiperidine obtained by the method described below.

b) A solution of 4.5 g of the methiodide of 3-ethylpyridine in 50 ml of anhydrous alcohol was shaken with hydrogen at room temperature in the presence of 0.3 g of platinum oxide (Adams' catalyst). When the required amount of hydrogen (1.325 liters) had been absorbed, the platinum black was filtered off and the alcohol solution evaporated in vacuum. The white crystalline residue of the hydroiodide was treated with excess 50% potassium hydroxide and the liberated oil extracted with ether. The ether solution was dried with potassium carbonate, the ether removed and the residue distilled at atmospheric pressure. We obtained 1.65 g (72%) of 1-methyl-3-ethylpiperidine (XIII). The colorless, volatile oil was readily soluble in organic solvents. The b. p. was 149-151° and the $n^{20}D$ 1.4460.

The methiodide was a white crystalline substance. The m.p. was 191-192° (from acetone).

The picrate formed yellow crystals. The m. p. was 130-132° (from alcohol).

Found %: C 47.08; H 5.65; N 15.55. $C_{14}H_{20}O_7N_4$. Calculated %: C 47.19; H 5.62; N 15.73.

Hofmann degradation of 1-azabicyclo-(3,2,1)-octane under different conditions. a) Distillation of the quaternary base (V) in vacuum. The quaternary base of 1-azabicyclo-(3,2,1)-octane (V), obtained by shaking an aqueous solution of 10 g of the methiodide (IV) with silver oxide, was heated in vacuum (50-55 mm). At a temperature of 140° (in the bath), the quaternary base began to decompose. The decomposition products distilled off at 66-77° (50-55 mm) and the distillate was saturated with dry potassium carbonate and extracted with ether. The ether solution was dried with potassium carbonate, the ether removed and the residue distilled at atmospheric pressure. We obtained 2.6 g (52%) of 1-methyl-3-allylpyrrolidine. The b. p. was 149-152° and the $n^{20}D$ 1.4462

b) Degradation of the methiodide of 1-azabicyclo-(3,2,1)-octane in the presence of alkali. 20 g of the methiodide of 1-azabicyclo-(3,2,1)-octane in 140 ml of 40% potassium hydroxide solution was boiled for 2 hours. The oil liberated was steam distilled and the distillate extracted with ether. The ether solution was dried with potassium carbonate, the ether removed and the substance distilled. We obtained 6.5 g (65%) of 1-methyl-3-allylpyrrolidine with b.p. 149-152° and 0.5 g (5%) of di[β-(1-methylpiperidyl-3)]-ethyl ether with b. p. 154-155° (5 mm).

c) Degradation of the quaternary base by heating with water under pressure. A solution of the quaternary base (V), obtained from 10 g of the methiodide of 1-azabicyclo-(3,2,1)-octane (IV), in 4 ml distilled water was heated in a sealed tube at 200° for 6 hours. The oil liberated was extracted with ether, the ether solution dried with potassium carbonate and the residue distilled. We obtained 0.9 g (18%) of 1-methyl-3-allylpyrrolidine with b. p. 149-152°, 0.4 g (8%) of di-[β-(1-methylpiperidyl-3)]-ethyl ether with b. p. 154-155° (5 mm) and 1.7 g (35%) of 1-methyl-3-(β-hydroxyethyl)-piperidine (IX) with b. p. 111-112° (5 mm) and n^{20}_D 1.4776. The latter was an immobile liquid, which was soluble in organic solvents and sparingly so in water.

Found %: C 66.92; H 11.90; N 9.72. $C_8H_{17}ON$. Calculated %: C 67.10; H 11.78; N 9.78.

The picrate formed yellow crystals. The m. p. was 144-145° (from alcohol).

The methiodide appeared as white crystals. The m. p. was 107-108° (from acetone).

Reaction of 1-methyl-3-(β-hydroxyethyl)-piperidine (IX) with hydrobromic acid. 1.5 g of 1-methyl-3-(β-hydroxyethyl)-piperidine and 25 ml of 67% hydrobromic acid were heated in a sealed tube at 100-110° for 6 hours. The reaction mixture was evaporated in vacuum and the solid residue recrystallized from acetone. We obtained 2.0 g (67%) of the hydrobromide of 1-methyl-3-(β-bromoethyl)-piperidine as white crystals, which were readily soluble in water, sparingly so in alcohol and acetone and insouble in ether. The m. p. was 134-136°. The substance did not depress the melting point of the hydrobromide of 1-methyl-3-(β-bromoethyl)-piperidine described above.

SUMMARY

1. It was established that a Hofmann degradation of 1-azabicyclo-(3,2,1)-octane under various conditions — at atmospheric pressure, in vacuum, in 40% potassium hydroxide solution and under pressure — gave three products: 1-methyl-3-allylpyrrolidine, 1-methyl-3-(β-hydroxyethyl)-piperidine and di[β-(1-methylpiperidyl-3)]-ethyl ether.

2. 1-Methyl-3-allylpyrrolidine was isolated in all cases and was the main degradation product of 1-azabicyclo-(3,2,1)-octane in an alkaline medium, in vacuum and at atmospheric pressure.

3. When 1-azabicyclo-(3,2,1)-octane was heated in water under pressure, the main decomposition product was 1-methyl-3-(β-hydroxyethyl)-piperidine.

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SYNTHESIS AND PROPERTIES OF PYRROLIDINE BASES

VI. 2-METHYL-N-ω-ALUMINOHEXYLPYRROLIDINE AND SOME OF ITS CONVERSIONS

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In a previous communication [1] we showed that the reaction of γ-acetopropyl alcohol with the formyl derivative of ethylene diamine led to the formation of 2-methyl-N-β-aminoethylpyrrolidine and 2,2-dimethyl-N,N'-dipyrrolidylethane. Some of the derivatives of the pyrrolidine bases obtained showed a considerable physioliogical activity.

In continuing our investigations we carried out the analogous reaction of γ-acetopropyl alcohol and hexamethylene diamine.

In the present communication we present the synthesis of 2-methyl-N-ω-aminohexylpyrrolidine and some of its conversions. In contrast to 2-methyl-N-β-aminoethylpyrrolidine, 2-methyl-N-ω-aminohexylpyrrolidine was not obtained by the reaction of γ-acetopropyl alcohol with the previously prepared formyl derivative of hexamethylene diamine, but by heating a mixture of γ-acetopropyl alcohol, hexamethylenediamine and formic acid. In addition to the main reaction product, 2-methyl-N-ω-aminohexylpyrrolidine (II) (70%), we also obtained 1,6-bis(2-methylpyrrolidyl-1)-hexane (III) (25%).
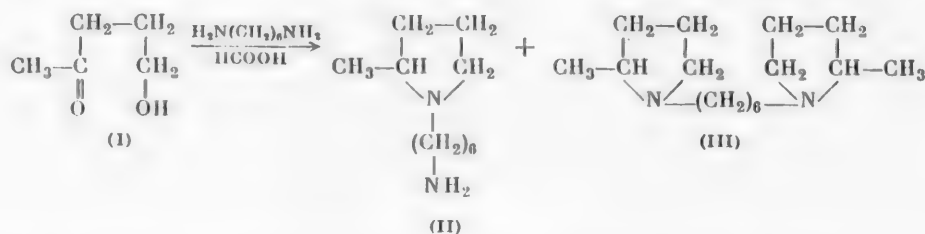
Preliminary tests of some of the derivatives of the pyrrolidine bases (II and III) obtained showed their considerable physiological activity.

We studied some conversions of 2-methyl-N-ω-aminohexylpyrrolidine (II) in order to obtain preparations of possible pharmacological activity. Reaction of (II) with furfural and benzaldehyde yielded Schiff's bases (IV and V), which were converted to the corresponding secondary amines (VI and VII) by reduction with magnesium in methyl alcohol [2] (by Zechmeister's method). Reaction of these secondary amines with benzyl chloride and with 2-methyl-N-β-chloroethylpyrrolidine gave us tertiary amines – N-2-furfuryl-N-benzyl-ω-(2-methylpyrrolidyl-1)-hexylamine (VIII) and N-benzyl-N-[(2-methylpyrrolidyl-1)-β-ethyl]-(2-methylpyrrolidyl-1)-hexylamine (IX). Reaction of (II) with ethylene oxide and propylene oxide yielded amino alcohols: N,N-β,β'-dihydroxydiethyl-ω-(2-methyl-N'-pyrrolidyl-1)-hexylamine (X) and N,N-β,β'-dihydroxydipropyl-ω-(2-methyl-N'-pyrrolidyl-1)-hexylamine (XI), which were then converted into the corresponding β-chloroalkylamines: N,N-(β,β'-dichlorodiethyl)-ω-(2-methylpyrrolidyl-1)-hexylamine (XII) and N,N-(β,β'-dichlorodipropyl)-ω-(2-methylpyrrolidyl-1)-hexylamine (XIII).

All the conversions mentioned may be represented by the following scheme:

R
NH—CH₂—⟨benzene⟩ ← R—N=CH—⟨benzene⟩ ← R(II)NH₂ → R—N=CH—⟨furan⟩ (IV) → R—NH—CH₂—⟨furan⟩ (VI)

(VII)   (V)   (II)

R—N(CH₂—C₆H₅)(CH₂—CH₂—N⟨2-methylpyrrolidine⟩)   (IX)

R—N(CH₂—⟨furan⟩)(CH₂C₆H₅)   (VIII)

R—N(CH₂CHOHCH₃)(CH₂CHOHCH₃) (XI) ← → R—N(CH₂CH₂OH)(CH₂CH₂OH) (X)

HCl·R—N(CH₂CHClCH₃)(CH₂CHClCH₃) (XIII)

HCl·R—N(CH₂CH₂Cl)(CH₂CH₂Cl) (XII)

$$R = \left[\begin{array}{c} CH_3 \\ N \\ (CH_2)_6 - \end{array} \right]$$
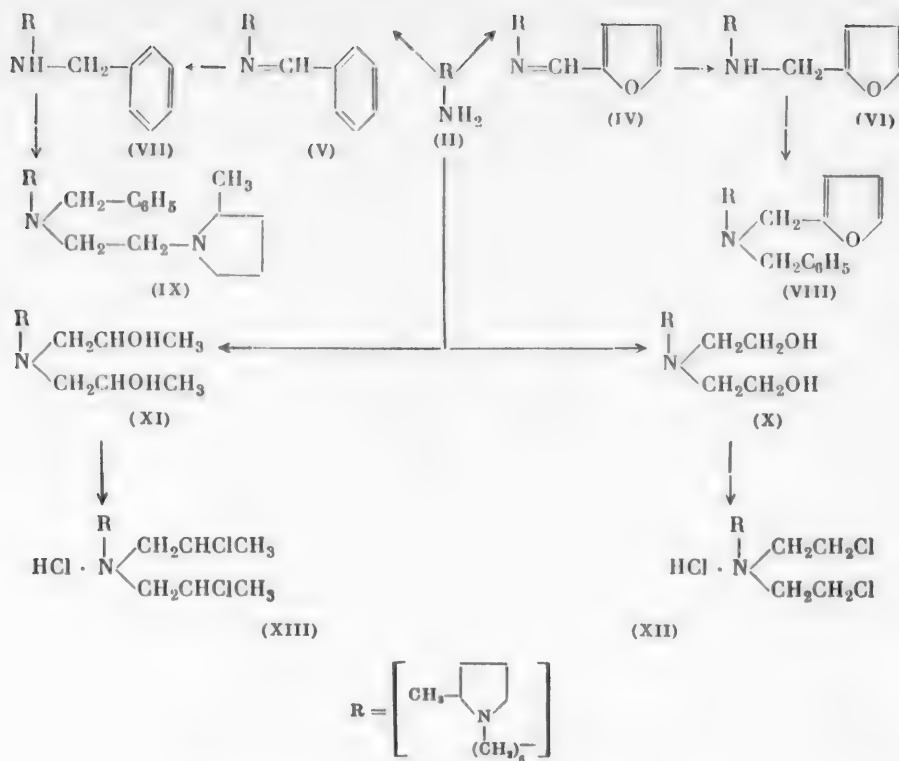
EXPERIMENTAL

Technical acetopropyl alcohol that had been vacuum distilled twice was used in the investigation.

B. p. 114-115° at 30 mm, $n^{20}D$ 1.4395, d^{20}_4 1.0068, MR_D 26.69. According to data [3]: b. p. 115-116° at 30 mm, $n^{20}D$ 1.4390.

2-Methyl-N-ω-aminohexylpyrrolidine (II) and 1,6-bis(2-methylpyrrolidyl-1)-hexane (III). Into a three-necked flask with a thermometer immersed in the liquid and a receiver was placed 40.8 g of γ-acetopropyl alcohol, 46.4 g of hexamethylenediamine, 37 g of ~85% formic acid and 2 g of powdered nickel (from nickel formate). When the mixture was heated to 115-120°, a reaction began with the voluminous evolution of carbon dioxide. Water and excess formic acid were distilled into the receiver. After 14 hours, even at 180° the evolution of carbon dioxide had almost ceased and then 20 ml of 85% formic acid was added and heating continued (12 hours). The reaction product was hydrolyzed by boiling (3.5 hours) with 150 ml of concentrated hydrochloric acid, neutralized with 40% sodium hydroxide solution, extracted with ether and fractionated in vacuum. We obtained the following fraction: 1st, 26 g (70.6%), substance (II) and the 2nd, 20 g (25%), substance (III).

Analysis of subst. (II): b. p. 116° (7 mm), $n^{20}D$ 1.4690, d^{20}_4 0.8803, MR_D 58.31; calc. 51.16.

Found %: C 76.75, 76.82; H 13.06, 13.09. $C_{11}H_{24}N_2$. Calculated %: C 76.67; H 13.13.

Analysis of subst. (III): b. p. 157-158° (7 mm), $n^{20}D$ 1.4725, d^{20}_4 0.8899, MR_D 79.47; calc. 79.57.

Found %: C 76.05, 76.01; H 12.90, 12.82. $C_{16}H_{32}N_2$. Calculated %: C 76.11; H 12.78.

The dimethiodide of (II) [4] had m. p. 170 - 172°; the dimethiodide of (III) had m. p. 223-225°.

2-Methyl-N-(ω-furfurylideneaminohexyl)-pyrrolidine (IV). A mixture consisting of 25 g of (II) and 14 g of freshly distilled furfural was kept at 35-40° for 4 hours and then fractionated in vacuum. We obtained 28 g (80%) of (IV).

B. p. 203-205° (15 mm), n^{20}D 1.5070, d^{20}_4 0.9677, MR$_D$ 79.81; calc. 79.47.

Found %: C 73.42, 73.36; H 10.18, 10.09. $C_{16}H_{26}ON_2$. Calculated %: C 73.24; H 9.99.

The dipicrate had m. p. 232-235°.

2-Methyl-N-(ω-benzylideneaminohexyl)-pyrrolidine (V). A mixture consisting of 18.6 g of (II) and 16.2 g of freshly distilled benzaldehyde was heated at 30-50° for 6 hours and then fractionated in vacuum. We obtained 24 g (88%) of (V).

B. p. 210-211° (10 mm), n^{20}D 1.5240, d^{20}_4 0.95233, MR$_D$ 87.52; calc. 86.60.

Found %: C 78.98, 79.17; H 10.61, 10.52. $C_{18}H_{28}N_2$. Calculated %: C 79.36; H 10.36.

The dipicrate had m. p. 228-230°.

2-Methyl-N-(ω-furfurylaminohexyl)-pyrrolidine (VI). To 12 g of purified magnesium in 180 ml of anhydrous methanol was added 20 g of (IV). After several minutes a vigorous reaction began and was complete in 30 minutes; the magnesium dissolved completely. The alcohol was removed in vacuum and the residue extracted several times with anhydrous benzene. The benzene extracts were fractionated. We obtained 10 g (50%) of (VI).

B. p. 208-209° (26 mm), n^{20}D 1.4890, d^{20}_4 0.9560, MR$_D$ 79.77; calc. 79.84.

Found %: C 72.75, 72.81; H 10.75, 10.64. $C_{16}H_{28}ON_2$. Calculated %: C 72.68; H 10.68.

2-Methyl-N-(ω-benzylaminohexyl)-pyrrolidine (VII). 15 g of (V) was reduced with 8.7 g of purified magnesium in 132 ml of anhydrous methanol. The reaction began after 10 minutes and continued for an hour. The alcohol was evaporated to dryness in vacuum and the residue extracted several times with anhydrous benzene. Fractionation yielded 9 g (53%) of (VII).

B. p. 178-179° (13 mm), n^{20}D 1.4875, d^{20}_4 0.90816, MR$_D$ 86.99; calc. 87.06.

Found %: C 78.91, 78.84; H 11.04, 10.96. $C_{18}H_{30}N_2$. Calculated %: C 78.75; H 11.02.

The dipicrate had m. p. 230-231° (from alcohol).

N-2-Furfuryl-N-benzyl-ω-(2-methylpyrrolidyl-1)-hexylamine (VIII). For the preparation we used a method described in the literature [5] for tertiary pyrrolidylethylamines. A mixture consisting of 5.28 g of (VI), 3.1 g of benzyl chloride and 5 g of anhydrous sodium carbonate was heated on an oil bath at 160° for 6 hours. The cooled reaction mixture was diluted with water and extracted with ether. After two distillations we obtained 4 g (57%) of (VIII).

B. p. 245-246° (13 mm), n^{20}D 1.5240, d^{20}_4 0.99123, MR$_D$ 109.43; calc. 109.00.

Found %: C 78.49, 78.44; H 9.64, 9.69. $C_{23}H_{34}ON_2$. Calculated %: C 77.91; H 9.62.

The dipicrate had m. p. 159-160°.

N-Benzyl-N-(2-methyl-β-ethylpyrrolidyl-1)- ω-(2-methylpyrrolidyl-1)-hexylamine (IX). As described above for (VIII), from 5.48 g of (VII), 3.53 g of 2-methyl-N- β-chloroethylpyrrolidene and 5.3 g of anhydrous sodium carbonate we obtained 6 g of (IX)(52%).

B. p. 259-260° (20 mm), n^{20}D 1.5100, d^{20}_4 0.9497, MR$_D$ 121.44; calc. 121.47.

Found %: C 77.98, 77.80; H 11.20, 11.16. $C_{25}H_{43}N_3$. Calculated %: C 77.86; H 11.24.

The tripicrate had m. p. 210-215°.

N,N-β,β'-Dihydroxydiethyl-ω-(2-methylpyrrolidyl-1)-hexylamine (X). 13.6 g of (II) was heated in an autoclave tube with 7 g of ethylene oxide and 1.4 g of water at 100° for 6 hours. The cooled reaction mixture was extracted with ether and the extracts dried and fractionated. Two vacuum distillations yielded 16 g (79%) of (XII).

B. p. 243-246° (18 mm), n^{20}D 1.4850, d^{20}_4 0.9895, MR$_D$ 78.90; calc. 80.20.

The dipicrate had m. p. 154-155°.

Found %: C 44.39, 44.39; H. 5.60, 5.77. $C_{27}H_{38}O_{18}N_3$. Calculated %: C 44.38; H 5.24.

N,N-β,β'-Dihydroxydipropyl-ω-(2-methylpyrrolidyl-1)-hexylamine (XI). As with (XII), we obtained 14 g (63%) of (XIII) from 13.6 g of (II), 8.6 g of propylene oxide and 1.4 g of water.

B. p. 225-226° (18 mm), n^{20}D 1.4780, d^{20}_4 0.9510, MR_D 89.40; calc. 89.43.

The dipicrate had m. p. 158-159°.

Found %: C 45.49, 45.61; H 5.68, 5.88. $C_{29}H_{42}O_{16}N_8$. Calculated %: C 45.90; H 5.58.

N,N-β,β'-Dichlorodiethyl-ω-(2-methylpyrrolidyl-1)-hexylamine. Dihydrochloride (XII). Into a three-necked flask, fitted with a mechanical stirrer, a reflux condenser and a dropping funnel, was placed 7 g of (XII) in 35 ml of chloroform. With cooling, 9.6 g of thionyl chloride in 20 ml of chloroform was gradually added to the mixture dropwise and then the mixture was kept at 45° for 2 hours. Removal of the excess thionyl chloride and the chloroform in vacuum yielded 10 g of an oil, which crystallized on long standing in a vacuum desiccator. The material was boiled with charcoal and recrystallized from anhydrous methanol to give 8.5 g (76.5%) of the dihydrochloride (XII) with m. p. 170-175° (decomp.).

Found %: C 47.26, 47.29; H 8.9, 8.76. $C_{15}H_{32}N_2Cl_4$. Calculated %: C 47.13; H 8.44.

N,N-β,β'-Dichlorodipropyl-ω-(2-methylpyrrolidyl-1)-hexylamine. Dihydrochloride (XIII). As described for (XII), from 4 g of (XI) and 4.86 g of thionyl chloride in 30 ml of chloroform we isolated 4.5 g of an oil, which crystallized on long standing in a vacuum desiccator. Purification yielded 3.9 g (72%) of (XIII).

Found %: C 50.95, 51.06; H 8.82, 8.77. $C_{17}H_{36}N_2Cl_4$. Calculated %: 50.91; H 8.84.

SUMMARY

The reaction of γ-acetopropyl alcohol with hexamethylenediamine-1,6 and formic acid gave 2-methyl-N-ω-aminohexylpyrrolidine (in 70%) and 1,6-bis(2-methylpyrrolidyl-1)-hexane (in 25% yield). A study was made of some of the conversions of 2-methyl-N-ω-aminohexylpyrrolidine.

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REACTIONS OF HYDRAZINE DERIVATIVES

XXII. 3-AMINO-1-ARYLPYRAZOLINES AND THEIR SALICYLAL DERIVATIVES

A. N. Kost, Yu. V. Konnova, V. V. Ershov and E. G. Rukhadze

We previously described the preparation of 3-amino-1-phenylpyrazolines (I) by the reaction of various β-substituted propionitriles with phenylhydrazine [1]. It was found that this aminopyrazoline (I), like certain other hydrazine derivatives, had a clearly expressed bacteriostatic action, suppressing the growth of the human tubercle bacillus. In connection with this, we synthesized a series of 3-amino-1-phenylpyrazolines by the reaction of α,β-unsaturated nitriles with arylhydrazines using the method of Duffin and Kendal [2].

(I) R = H, R' = H; (II) R = CH$_3$, R' = H; (III) R = H, R' = CH$_3$; (IV) R = H, R' = C$_6$H$_5$;
(V) R = H, R' = p-CH$_3$C$_6$H$_4$.
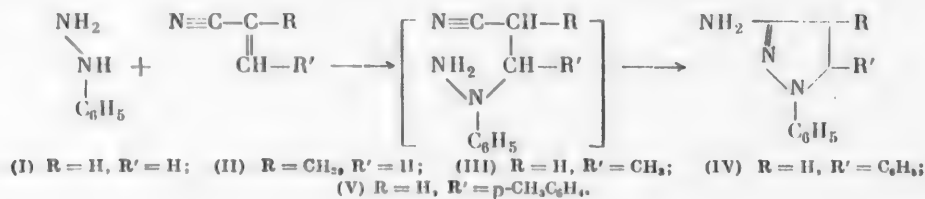
The first part of this reaction is apparently the addition of the unsaturated nitrile, which is followed by cyclization. This is confirmed by the fact that the nitrile group reacts with hydrazine only under comparatively drastic conditions, while acrylonitrile readily cyanoethylates phenylhydrazine in alkaline media, when the cyanoethyl group is added to that nitrogen atom to which the phenyl radical is attached [3]. We should note that by strictly following the procedure of Duffin and Kendal [2] we obtained variable and, as a rule, low yields of the aminopyrazolines (the above authors also quote the same yields). It was found that the reaction was better performed in the higher boiling butyl alcohol instead of ethyl. As catalyst we used sodium butylate and not sodium ethylate. It was also found necessary to use larger amounts of the sodium alcoholate than those used by Duffin and Kendall. All this raised the yields of the aminopyrazolines by 20-40% and they reached 50-80% of theoretical.

We prepared 3-amino-1-p-tolylpyrazoline (VI) by reacting β-dimethylaminopropionitrile with p-tolylhydrazine. In several attempts to carry out a reaction between phenylhydrazine and the nitrile of p-nitrocinnamic acid, we observed the strong evolution of heat accompanied by tar formation. The same was observed on reacting acrylonitrile with p-nitrophenylhydrazine or m-nitro-p-tolylhydrazine and also the nitrile of m-nitrocinnamic acid with phenylhydrazine. Apparently, the reaction between nitro and hydrazino groups, which was reported previously [4], occurs in strongly alkaline media with heating.

Bacteriological tests* in vitro showed that the highest activity against human tubercle bacilli was possessed by 1-phenyl-3-aminopyrazoline (I), which suppressed the growth of this bacillus at a dilution of 1 : 1024000. It acted more weakly (at a dilution of 1 : 128000) on the avian tubercle bacillus and acidoresistant saprophytes (1 : 64000) and, finally, at dilution of 1 : 2000 to 1 : 8000 it showed a bacteriostatic action against pathogenic fungi, actinomyces, streptococci and staphylococci. However, when horse serum was added, the activity of this

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*The test were performed by S. N. Milovanova in the S. Ordzhonikidze All-Union Institute of Chemical Pharmaceutics.
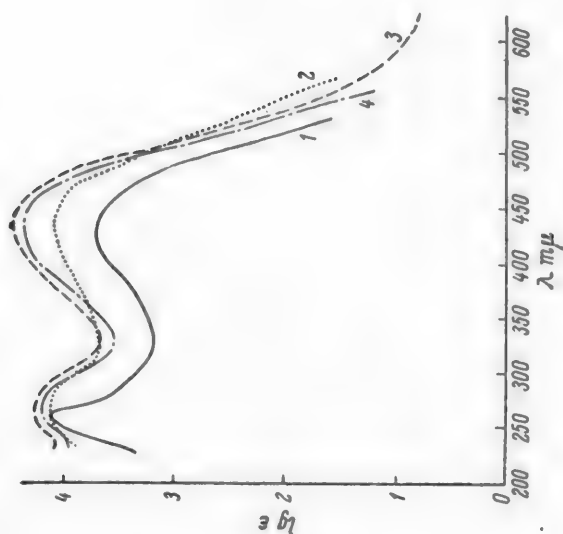
Fig. 1. Absorption spectra of 3-salicylalimino-1-phenylpyrazolines. 1) 3-salicylalimino-1-phenyl-pyrazoline; λ_{max} 262, 430 mμ, lgε 4.139, 3.722; 2) 3-salicylalimino-4-methyl-1-phenylpyrazoline; λ_{max} 260, 430 mμ, lgε 4.123, 4.086; 3) 3-salicylalimino-5-methyl-1-phenylpyrazoline; λ_{max} 262, 430 mμ, lgε 4.294, 4.477; 4) 3-salicylalimino-1,5-diphenylpyrazoline: λ_{max} 258, 430 mμ, lgε 4.214, 4.361.
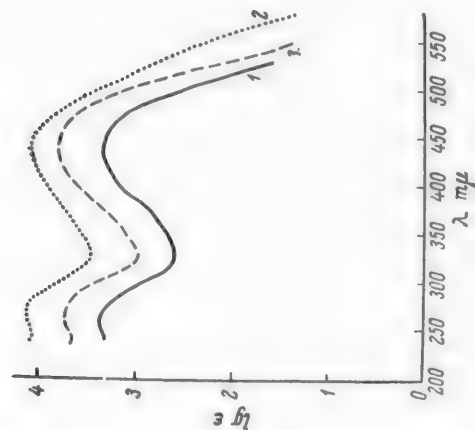
Fig. 2. Absorption spectra of 3-(5-bromo-salicylalimino)-1-phenylpyrazolines. 1) 3-(5-bromosalicylalimino)-1-phenylpyrazoline; λ_{max} 256, 440 mμ, lgε 3.378, 3.371; 2) 3-(5-bromosalicylalimino)-4-methyl-1-phenylpyrazoline; λ_{max} 260, 440 mμ, lgε 4.149, 4.127; 3) 3-(5-bromosalicylalimino)-1,5-diphenylpyrazoline: λ_{max} 263, 440 mμ, lgε 3.757, 3.854.
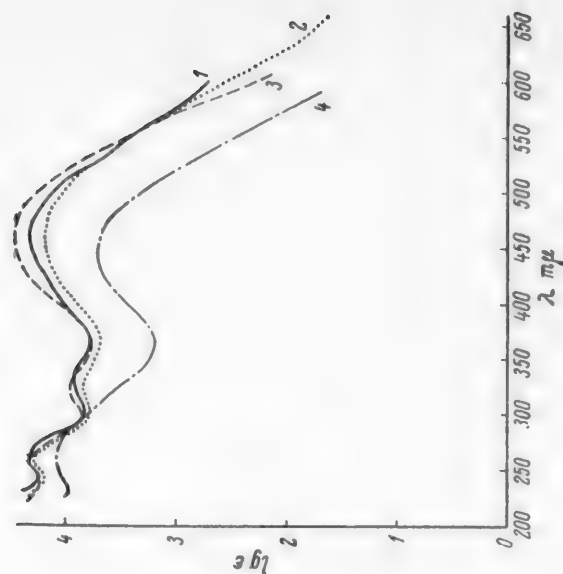
Fig. 3. Absorption spectra of 3-(2-hydroxynaphthalimino)-1-phenylpyrazolines. 1) 3-(2-hydroxynaphthalimino)-1-phenylpyrazoline; λ_{max} 258, 326, 460 mμ, lgε 4.307, 3.897, 4.296; 2) 3-(2-hydroxynaphthalimino)-4-methyl-1-phenylpyrazoline; λ_{max} 260, 326, 460 mμ lgε 4.276, 3.820, 4.152; 3) 3-(2-hydroxynaphthalimino)-5-methyl-1-phenylpyrazoline; λ_{max} 260, 328, 460 mμ, lgε 4.307, 3.940, 4.433; 4) 3-(2-hydroxynaphthalimino)-1,5-diphenylpyrazoline: λ_{max} 263, 450 mμ, lgε 4.089, 3.680.

substance against the human tubercle bacillus fell to a dilution of 1 : 16000, which makes it unsuitable for clinical use. The other aminopyrazolines and also the acetyl derivative of 1-phenyl-3-aminopyrazoline had a similar, but considerably weaker action against the human tubercle bacillus, namely, compounds (IV) and (VI) were active in dilutions of 1 : 64000 and 1 : 25600, respectively. The rest only had a bacteriostatic action at dilutions of 1 : 8000. At dilutions of 1 : 2000, all the preparations suppressed the growth of pathogenic fungi. Compounds (II)and (V) were slightly more active and suppressed the growth of Microsporon and Achorion at a dilution of 1 : 16000. As regards coccal bacteria, bacteriostatic action was observed at dilutions of not greater than 1 : 8000. None of the preparations had any effect on the growth of Proteus vulgaris bacilli at a dilution of 1 : 1000.

The 3-aminopyrazolines obtained reacted readily with salicylaldehyde, and 5-bromosalicylaldehyde and slightly less readily with 2-hydroxynaphthaldehyde to form the corresponding brightly colored salicylalimines. The ultraviolet absorption spectra * of the 3-(2-hydroxynaphthalimino)-pyrazolines have three maxima while the rest have two. The first maximum for all the imines lies in the range 258-260 mμ and the second is characteristic of the hydroxyaldehyde component and for the salicylal, 5-bromosalicylal and 2-hydroxynaphthal derivatives they lie at 430, 440 and 450-460 mμ, respectively (see Fig. 1-3). This observation is interesting since pyrazoline systems without functional groups do not have characteristic absorption spectra [5].

Like the normal N-substituted salicylalimines, which are widely used in analytical chemistry [6], the salicylalimines obtained could give internal complexes which in this case, were formed not only through the imino nitrogen but also with the participation of the nitrogen in the pyrazoline ring. It was found that almost all the salicylaliminopyrazolines tested gave precipitates or a green color with ferric salts; many gave characteristic precipitates with salts of Cu^{+2}, Ni^{+2}, Co^{+2}, Zn^{+2}, Pb^{+2}, and Be^{+2}. The hydroxyaldehyde derivatives of 3-amino-5-methyl-1-phenylpyrazoline were the most interesting. Thus, its salicylal derivative readily precipitated cadmium ions; the 2-hydroxynaphthaldehyde derivative was of interest as a reagent for cobalt as it formed a red, amorphous precipitate with cobaltous salts and did not precipitate nickel salts under the same conditions.

Our attempts to condense aminopyrazolines with o-hydroxyketones (o-hydroxyacetophenone and o-hydroxybutyrophenone) were unsuccessful. The reaction did not occur under the normal conditions.

EXPERIMENTAL

3-Amino-1-phenylpyrazoline (I). 4 g of sodium was dissolved in 100 ml of butyl alcohol and 44 g of phenylhydrazine and 25.7 g of acrylonitrile were added. The mixture was boiled for 5 hours. The cooled solution deposited a precipitate of 3-amino-1-phenylpyrazoline, which was filtered off, washed with water and ethyl alcohol and recrystallized from acetone. The yield wag 48 g (74%) and the m.p. 169° [1, 2].

3-Salicylalimino-1-phenylpyrazoline. A solution of 1.1 g of 3-amino-1-phenylpyrazoline (I and 2.5 g of salicylaldehyde in 5 ml of dioxane was boiled for 15 minutes. The bright red crystals, which were deposited on cooling, were filtered off and recrystallized from dioxane. The yield was 1.3 g (80%) and the m. p. 228° (decomp.). **

3-(2-hydroxynaphthalimino-1)-1-phenylpyrazoline. The substance was prepared similarly from 1.1 g of aminopyrazoline (I) and 3.2 g of 2-hydroxynaphthaldehyde-1 in 20 ml of dioxane by boiling for 30 minutes. The yield was 2 g (35%) and the m.p. 204° (from dioxane).

Found %: C 76.14, 76.21; H 5.65, 5.66. $C_{20}H_{17}ON_3$. Calculated %: C 76.17; H 5.43.

3-(5-bromosalicylalimino)-1-phenylpyrazoline. Boiling 2.75 g of aminopyrazoline (I) and 3.5 g of 5-bromosalicylaldehyde in 15 ml of ethyl alcohol for 15 minutes yielded 5.6 g of (88.8%) of imine with m. p. 205-206° (from alcohol).

Found %: N 12.03, 11.95. $C_{16}H_{14}ON_3Br$. Calculated %: N 12.20.

* The absorption spectra were plotted by L. L. Polstyanko on an SF-4 spectrophotometer. The solvent was methyl alcohol.

** In a previous communication [1] the m. p. of 3-salicylalimino-1-phenylpyrazoline was reported as 128° instead of 228° by mistake.

3-Amino-4-methyl-1-phenylpyrazoline (II). 4 g of sodium was dissolved in 100 ml of butyl alcohol and 44 g of phenylhydrazine and 25 g of methacrylonitrile added. The mixture was boiled for 6 hours. The cooled mixture deposited a precipitate of 3-amino-4-methyl-1-phenylpyrazoline (II), which was filtered off, washed with water and recrystallized from petroleum ether. The m. p. was 82° [2] and the yield 39 g (60%).

3-Salicylalimino-4-methyl-1-phenylpyrazoline. This substance was prepared by boiling a solution of 1.4 g of aminopyrazoline (II) and 2.44 g of salicylaldehyde in 5 ml of ethyl alcohol for 30 minutes. The yield was 1.5 g (68%) and the m. p. 113-114° (from alcohol).

Found %: N 14.61, 14.78. $C_{17}H_{17}ON_3$. Calculated %: N 15.04.

3-(2-Hydroxynaphthalimino-1)-4-methyl-1-phenylpyrazoline. Boiling (30 minutes) 2.8 g of aminopyrazoline (II) and 6.3 g of 2-hydroxynaphthaldehyde-1 in 20 ml of ethyl alcohol yielded 2.9 g (58%) of imine with m. p. 128-129° (from alcohol).

Found %: C 76.43; H 6.02. $C_{21}H_{19}ON_3$. Calculated %: C 76.56; H 5.81.

3-(5-Bromosalicylalimino)-4-methyl-1-phenylpyrazoline. This substance was obtained by boiling for 15 minutes a mixture of 1.4 g of pyrazoline (II) and 1.6 g of 5-bromosalicylaldehyde in 10 ml of alcohol. The yield was 2.0 g (80%) and the m. p. 140-141° (from dioxane).

Found %: N 11.67, 11.76. $C_{17}H_{16}ON_3Br$. Calculated %: N 11.73.

3-Amino-5-methyl-1-phenylpyrazoline (III). 1.5 g of sodium was dissolved in 37 ml of ethyl alcohol and 16.2 g of phenylhydrazine and 10 g of cis-crotononitrile added. The mixture was boiled until crystals of the aminopyrazoline (III) precipitated (5 hours) and these were then filtered off, washed with water and recrystallized from ethyl alcohol. The yield was 12.8 g (50%) and the m. p. 105-106° [2].

3-Salicylalimino-5-methyl-1-phenylpyrazoline. This substance was prepared by boiling 1.4 g of pyrazoline (III) and 2.44 g of salicylaldehyde in 10 ml of alcohol for 30 minutes. The yield was 1.3 g (58%) and the m. p. 135-136° (from a mixture of ethyl alcohol and dioxane).

Found %: N 14.63, 14.69. $C_{17}H_{17}ON_3$. Calculated %: N 15.04.

3-(2-Hydroxynaphthalimino-1)-5-methyl-1-phenylpyrazoline. This substance was prepared by boiling 1.4 g of pyrazoline (III) and 3.15 g of 2-hydroxynaphthaldehyde-1 in 10 ml of alcohol for 30 minutes. The yield was 1.75 g (70%) and the m. p. 164-165° (decomp., after recrystallization from a mixture of ethyl alcohol and dioxane).

Found %: N 13.09, 13.19. $C_{21}H_{19}ON_3$. Calculated %: N 13.06.

3-Amino-1,5-diphenylpyrazoline (IV). 2 g of sodium was dissolved in 50 ml of butyl alcohol and 18.2 g of phenylhydrazine and 24 g of the nitrile of trans-cinnamic acid were added. Crystals were immediately deposited and these were filtered off and recrystallized from ethyl alcohol. The yield was 34.5 g (86.3%) and the m. p. 194-195° [2].

3-Salicylalimino-1,5-diphenylpyrazoline. This substance was prepared by boiling 1.9 g of pyrazoline (IV) and 2.44 g of salicylaldehyde in 10 ml of ethyl alcohol for 30 minutes. The yield was 1.2 g (86%) and the m. p. 180-181° (decomp., from dioxane).

Found %: N 12.53, 12.80. $C_{22}H_{19}ON_3$. Calculated %: N 12.31.

3-(2-Hydroxynaphthalimino-1)-1,5-diphenylpyrazoline. The material was formed by boiling 1.9 g of pyrazoline (IV) and 3.15 g of 2-hydroxynaphthaldehyde-1 in 10 ml of ethyl alcohol for 30 minutes. The yield was 1.8 g (60%) and the m. p. 153-155° (from dioxane).

Found %: N 10.93, 11.12. $C_{26}H_{21}ON_3$. Calculated %: N 10.73.

3-(5-Bromosalicylalimino)-1,5-diphenylpyrazoline. The substance was prepared by boiling 1.79 g of pyrazoline (IV) and 1.6 g of 5-bromosalicylaldehyde in 5 ml of ethyl alcohol for 15 minutes. The yield was 1.45 g (83%) and the m. p. 135-136° (from alcohol).

Found %: N 9.80, 10.08. $C_{22}H_{18}ON_3Br$. Calculated %: N 9.99.

3-Amino-1-phenyl-5-p-tolylpyrazoline (V). 0.05 g of sodium was dissolved in 2 ml of ethyl alcohol and 0.5 g of phenylhydrazine and 0.6 g of the nitrile of p-methylcinnamic acid added. The mixture was boiled for 4 hours. The cooled solution deposited a precipitate, which was filtered off and recrystallized from alcohol. We obtained 0.85 g (81%) of the aminopyrazoline (V) with m. p. 139-140°.

Found %: N 17.10, 17.23. $C_{16}H_{17}N_3$. Calculated %: N 16.65.

3-Amino-1-p-tolylpyrazoline (VI). 0.5 g of sodium was dissolved in 25 ml of butyl alcohol and then 12.2 g of p-tolylhydrazine and 9.8 g of β-dimethylaminopropionitrile added. The mixture was boiled for 4.5 hours. The cooled mixture deposited a precipitate of 3-amino-1-p-tolylpyrazoline. The yield was 6 g (32%) and the m. p. 142° (from alcohol) [2].

SUMMARY

1. A series of 3-amino-1-phenylpyrazolines was synthesized and their bacteriostatic action investigated.

2. A description is given of the preparation of some 3-salicylalimino-1-phenylpyrazolines, which form internal complexes with some metal cations.

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SYNTHESIS OF ESTERS OF SOME PHOSPHINIC AND PHOSPHORIC ACIDS

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In a patent [1], Gresham reported that dioxolanes are readily cleaved by the action of acyl chlorides to form acyl derivatives of hydroxyhalo ethers.

$$
\begin{array}{l} CH_2-O \\ | \quad\quad\ \ \searrow CH_2 + CH_3COCl \rightarrow CH_3COO-CH_2CH_2-O-CH_2Cl. \\ CH_2-O \end{array}
$$
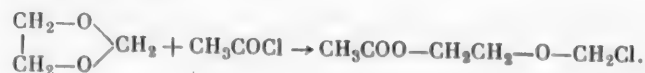
One would expect that other acid halides such as, for example, the acid halides of dialkylphosphoric acids, would also cleave the dioxolane ring in a similar way. In this way one would readily obtain esters of phosphoric acid with a reactive halogen atom in the ester radical.

$$
\begin{array}{l} CH_2-O \\ | \quad\quad\ \ \searrow CH_2 + (RO)_2P-Cl \rightarrow (RO)_2P-O-CH_2-CH_2-O-CH_2Cl \\ CH_2-O \qquad\qquad\ \|\qquad\qquad\qquad\ \| \\ \qquad\qquad\qquad\quad\ O \qquad\qquad\qquad\ O \end{array}
$$
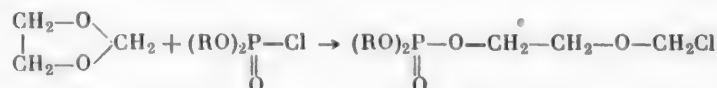
Experiment, however, showed that the reaction of dioxolane with the acid chloride of dialkylphosphoric acid did not proceed in the desired direction.

The accessibility of β-acetoxyethyl chloromethyl ether impelled us to use it for the synthesis of the corresponding esters of phosphinic acid. As experiment showed, the full esters of phosphorous acid reacted with β-acetoxyethyl chloromethyl ether smoothly by the scheme:

$$
\begin{array}{l} (RO)_3P + CH_2Cl-O-CH_2-CH_2-OCOCH_3 \rightarrow \\ \rightarrow (RO)_2P-CH_2-O-CH_2-CH_2-OCOCH_3 + RCl, \\ \qquad\quad \| \\ \qquad\quad O \end{array}
$$

where $R = C_2H_5$, C_3H_7-n & C_4H_9-n.
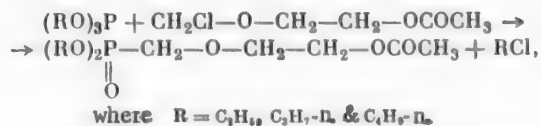
The constants of the esters obtained are presented in the table.

R	B. p. (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calc.	Yield (in %)
Ethyl	136—137.5°(1.5)	1.1491	1.4388	58.15	57.93	60
n-Propyl	160 (3)	1.0959	1.4400	67.88	67.16	66
n-Butyl	172—173 (2)	1.0685	1.4433	77.06	76.40	53

Many of the esters of thiophosphoric acid are good contact insecticides. Therefore, the preparation of esters with an acetoxyethoxymethyl radical was of definite interest from this point of view. However, it was not possible to prepare esters of thiophosphoric acid with a β-acetoxyethoxymethyl radical in a pure form by direct interaction of the chloro ether with the sodium salt of diethylthiophosphoric acid. The reaction product could not be distilled without decomposition.

The esters of phosphoric and thiophosphoric acids with heterocyclic radicals attract considerable attention at the present time since some of them are excellent insecticides [2]. In continuing our investigations on esters with heterocyclic radicals [2, 3], we synthesized mixed esters of phosphoric acid with thiazole and thiodiazole radicals. The reaction of the acid chloride of diethylphosphoric acid with the sodium salt of 4-methyl-2-hydroxythiazole gave a good yield of the corresponding mixed ester of phosphoric acid.

$$CH_3-C——N \qquad O \qquad CH_3-C——N \qquad O$$
$$CH \quad C-ONa + Cl-P(OC_2H_5)_2 \quad \rightarrow \quad CH \quad C-O-P(OC_2H_5)_2 + NaCl.$$
$$\diagdown S \diagup \qquad\qquad \diagdown S \diagup$$
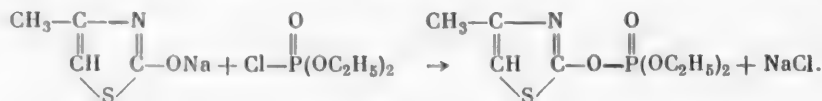
The ester was a liquid which distilled in vacuum without decomposition.

B. p. 153.5° (4 mm), $n^{20}D$ 1.4829, d^{20}_0 1.2305, MR_D 59.53; calc. 59.74.

The corresponding n-butyl and isobutyl esters did not distill without decomposition.

The mixed diethyl-methylthiazole ester of thiophosphoric acid was prepared by the action of the sodium salt of 4-methyl-2-hydroxythiazole on the acid chloride of diethylthiophosphoric acid, but could not be obtained in an analytically pure form as it did not distill in vacuum without decomposition.

The action of the acid chloride of diethylphosphoric acid on 4-methyl-2-aminothiazole yielded the corresponding substituted amide. In the pure form, the amide appeared as a crystalline substance with m. p. 124-126°.

$$CH_3-C——N \qquad O \qquad CH_3-C——N \qquad O$$
$$CH \quad C-NH_2 + Cl-P(OC_2H_5)_2 \quad \rightarrow \quad CH \quad C-NH-P(OC_2H_5)_2$$
$$\diagdown S \diagup \qquad\qquad \diagdown S \diagup$$
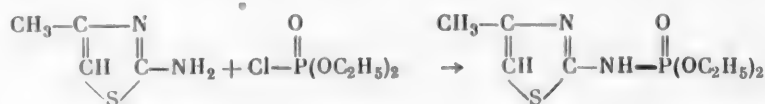
The amide could be obtained in an analytically pure form by distillation in vacuum, which was accompanied by large losses (b. p. 170-172° at 2 mm).

The reaction of hydrazine sulfate with carbon disulfide readily yields 2,5-dimercaptothio-3,4-diazole [4]. The accessibility of dimercaptothiodiazole stimulated us to study its reaction with acid chloride of diethylphosphoric acid.

$$N——N \qquad\qquad\qquad N——N$$
$$2(C_2H_5O)_2PCl + SH-C \quad C-SH \rightarrow (C_2H_5O)_2P-S-C \quad C-S-P(OC_2H_5)_2.$$
$$\| \qquad\qquad \diagdown S \diagup \qquad\qquad \| \qquad \diagdown S \diagup \qquad \|$$
$$O \qquad\qquad\qquad\qquad\qquad O \qquad\qquad\qquad\qquad O$$
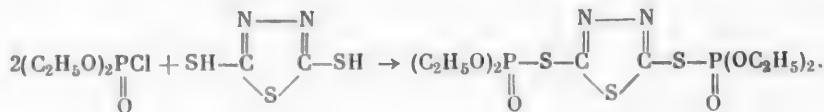
The reaction product did not distill in vacuum without decomposition. However, good analytical data, indicating its formation, were obtained without distillation.

EXPERIMENTAL

Reaction of acetyl chloride with dioxolane. 17.4 g of acetyl chloride was added dropwise to 16.4 g of dioxolane. No exothermic reaction was observed. The reaction mixture was then heated on a water bath at 70-80° for 3 hours and vacuum distilled. We obtained 23.5 g (69.2%) of β-acetoxyethyl chloromethyl ether.

B. p. 70-72° (4.5 mm), $n^{20}D$ 1.4373, d^{20}_0 1.1895, MR_D 33.62. $C_5H_9O_3Cl$. Calculated 33.45.

Reaction of the acid chloride of diethylphosphoric acid with dioxolane. 10.7 g of dioxolane was added from a dropping funnel to 16.6 g of the acid chloride of diethylphosphoric acid; no change was observed during this. The reaction mixture was then heated on a boiling water bath for 2 hours. Again no reaction was observed. Then 0.5 g of aluminum trichloride was added. The temperature of the reaction mixture rose from 15 to 23° and frothing was observed. The reaction mixture was heated on a boiling water bath for 8 hours. A colloidal precipitate of $Al(OH)_3$ was formed. After being centrifuged, the reaction mixture was vacuum distilled. We obtained the following fractions: 1st 64-66° (12.5 mm), $n^{20}D$ 1.4233, 0.8 g; 2nd 94-96° (12.5 mm), $n^{20}D$ 1.4263, 1.1 g; 3rd 128-131° (3 mm), $n^{20}D$ 1.4243, d^{20}_0 1.1755, 0.8 g.

Found %: P 17.53, 16.85. $C_7H_{16}O_5ClP$. Calculated %: P 12.56.

Reaction of triethyl phosphite with β-acetoxyethyl chloromethyl ether. 21 g of triethyl phosphite was added dropwise to 20 g of β-acetoxyethyl chloromethyl ether in an Arbuzov flask; the temperature of the reaction mixture rose to 42°. The reaction mixture was then heated on an oil bath at 120°. A vigorous reaction began immediately and the temperature of the reaction mixture rose to 140°, staying there even when the flask was removed from the bath. When the reaction had slowed down, the reaction mixture was heated at 120° again for 0.5 hour. Ethyl chloride was evolved. Two distillations from an Arbuzov flask yielded 20 g (60%) of the diethyl ester of β-acetoxyethoxymethylphosphinic acid.

B. p. 136-137.5° (1.5 mm), $n^{20}D$ 1.4388, d^{20}_0 1.1491, MR_D 58.15; calc. 57.93.
Found %: P 12.84, 12.96. $C_9H_{19}O_6P$. Calculated %: P 12.19.

Reaction of n-tributyl phosphite with β-acetoxyethyl chloromethyl ether. n-Tributyl phosphite was added dropwise to 17.5 g of β-acetoxyethyl chloromethyl ether in an Arbuzov flask. The temperature of the reaction mixture was kept at 24°. The mixture was then heated to 140° on an oil bath, when butyl chloride distilled off at 77-78° (6.5 g; theoretical, 10.6 g). After distilling the product twice from an Arbuzov flask, we obtained 18.7 g (53%) of the n-dibutyl ester of β-acetoxyethoxymethylphosphinic acid.

B. p. 172-173° (2 mm), $n^{20}D$ 1.4433, d^{20}_0 1.0685, MR_D 77.06; calc. 76.40.
Found %: P 10.94, 11.03. $C_{13}H_{27}O_6P$. Calculated %: P 9.99.

Reaction of n-tripropyl phosphite with β-accoxyethyl chloromethyl ether. 29.3 g of n-tripropyl phosphite was added dropwise to 21.2 g of β-acetoxyethyl chloromethyl ether in an Arbuzov flask. During this time the temperature of the reaction mixture was 23-25°. The mixture was heated on an oil bath (180-200°) and n-propyl chloride distilled off at 47°. After distilling the product three times from an Arbuzov flask, we obtained 24.5 g (66%) of the n-dipropyl ester of β-acetoxyethoxymethylphosphinic acid.

B. p. 160° (3 mm), $n^{20}D$ 1.4400, d^{20}_0 1.0959, MR_D 67.88; calc. 67.16.
Found %: P 11.01, 11.37. $C_{11}H_{23}O_6P$. Calculated %: P 10.98.

Reaction of diethylphosphoryl chloride with the sodium salt of 4-methyl-2-hydroxythiazole. 13.6 g of diethylphosphoryl chloride was added dropwise to a solution of 10.5 g of the sodium salt of 2-hydroxy-4-methyl-thiazole [5] in absolute acetone in a flask with a reflux condenser and a stirrer; the reaction mixture evolved heat. It was then heated on a boiling water bath for 3 hours. Afterward, the precipitate of sodium chloride (4.2 g) was filtered off and washed with dry acetone. The acetone was removed from the filtrate and the residue distilled in vacuum. We isolated 15.3 g (77.2%) of the diethyl ester of methylhydroxythiazole phosphoric acid.

B. p. 153.5° (4 mm), $n^{20}D$ 1.4829, d^{20}_0 1.2305, MR_D 59.74; calc. 59.53.
Found %: P 12.21, 12.07. $C_8H_{14}O_4NPS$. Calculated %: P 12.33.

Reaction of diethylphosphoryl chloride with 4-methyl-2-aminothiazole. 22.6 g of diethylphosphoryl chloride was added dropwise to a solution of 30 g of 4-methyl-2-aminothiazole [6] in benzene in a flask with a reflux condenser and a stirrer and during this procedure, the reaction mixture heated up to 30-35° and a white precipitate of methylaminothiazole hydrochloride (15.5 g; theoretical, 19.8 g) formed. Then the reaction mixture was heated for 3 hours at the boiling point of benzene. The precipitate was filtered off and washed with benzene and the benzene evaporated. The remaining thick, dark yellow liquid distilled poorly in vacuum with decomposition. A large residue remained. The distillation yielded the amide with b. p. 170-172° (2 mm) and which crystallized as regular prisms with m.p. 124-126°.

Found %: P 13.09, 12.95. $C_3H_{15}O_3N_2PS$. Calculated %: P 12.39.

Preparation of 2,5-dimercaptothio-3,4-diazole [4]. A solution of 20 g of carbon disulfide in 35 ml of ethyl alcohol was added dropwise to a solution of 10 g of hydrazine sulfate in 100 ml of water in a 0.5 liter round-bottomed flask, with a reflux condenser and a mechanical stirrer, which was cooled with water. Then a solution of 11 g of potassium hydroxide in 50 ml of ethyl alcohol was carefully added with cooling in snow. The reaction mixture was heated on a water bath for 2.5 hours. After this, an equal volume of concentrated hydrochloric acid was added to the filtrate. A white crystalline precipitate of 2,5-dimercaptothio-3,4-diazole formed. Drying this in a vacuum desiccator yielded 7.2 g (63%) of 2,5-dimercaptothio-3,4-diazole with m.p. 164-170°.

Reaction of diethylphosphoryl chloride with 2,5-dimercaptothio-3,4-diazole. 23 g of diethylphosphoryl chloride was added dropwise to a solution of 10 g of 2,5-dimercaptothio-3,4-diazole and 13.4 g of triethylamine in benzene. The reaction mixture gave off heat and deposited a precipitate of triethylamine hydrochloride, which was separated quantitatively by freezing. After 5 hours heating at 120° and then removal of the benzene, a thick yellow liquid (24 g) was left.

Found %: P 15.14, 14.96. $C_{10}H_{20}O_6N_2S_3P_2$. Calculated %: P 14.67.

It was not possible to isolate the product by distillation as it could not be distilled without decomposition. The product was analyzed without distillation.

SUMMARY

Esters of β-acetoxyethoxymethylphosphinic acid were synthesized by the action of chloromethyl 1-acetoxyethyl ether on trialkyl phosphites.

Some esters of phosphoric and thiophosphoric acid, containing heterocyclic radicals were synthesized.

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THE REACTION OF PHOSGENE AND OXALYL CHLORIDE WITH ESTERS OF PHOSPHOROUS ACID
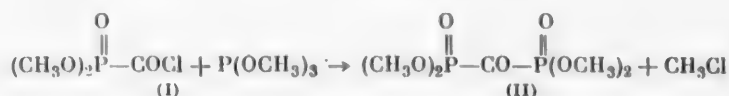
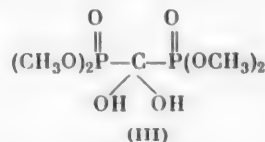A. N. Pudovik and R. N. Platonova

Kazan State University

The reactions of acid chlorides of monobasic carboxylic acids with the full esters of phosphorous acid were studied by M. I. Kabachnik and P. A. Rossiiskaya [1]. Later, the reactions of the acid chlorides of higher monobasic carboxylic acids with triethyl phosphite were carried out [2].

The possibility of replacing acid chlorides by acid anhydrides in preparing ketophosphinic esters by A. E. Arbuzov's reaction, was demonstrated by G. Kh. Kamai and V. A. Kukhtin [3]. Ketophosphinic esters are also formed by the action of cyclohexenyl acetate on dialkylphosphorous acids [4]. In the action of phosphites on acid halides of α-halogen substituted carboxylic acids, the reaction proceeds according to the Arbuzov rearrangement in the first stage and then anomalously in the second stage with the formation of unsaturated esters of phosphoric acid [5].

An article published recently [6] described the reaction of trimethylphosphite with phosgene. The authors considered that this reaction gave the methyl ester of chloroformylphosphinic acid (I), which then reacted with a second phosphite molecule to give an ester of carbonylphosphinic acid (II).

$$\underset{\text{(I)}}{(CH_3O)_2\overset{\overset{\displaystyle O}{\|}}{P}-COCl} + P(OCH_3)_3 \rightarrow \underset{\text{(II)}}{(CH_3O)_2\overset{\overset{\displaystyle O}{\|}}{P}-CO-\overset{\overset{\displaystyle O}{\|}}{P}(OCH_3)_2} + CH_3Cl$$

According to their data, (II) was not a compound with sharply expressed carbonyl reactions; it did not form a nitrophenylhydrazone or a semicarbazone but gave a stable, uncrystallizable hydrate (III) with water.

$$\underset{\underset{\text{(III)}}{\overset{\displaystyle OH \quad OH}{}}}{(CH_3O)_2\overset{\overset{\displaystyle O}{\|}}{P}-C-\overset{\overset{\displaystyle O}{\|}}{P}(OCH_3)_2}$$

The authors confirmed the structures of the compounds obtained only by calculating the molecular refraction for them and by elementary analysis data. *

In connection with our previous investigations of the reaction of phosphites with acid halides of α-halogen substituted carboxylic acids, it seemed interesting to us to study in more detail the reaction of phosphites with acid halides of dibasic acids.

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*Footnote in correction. In a short communication just published (Bull. Acad. Sci. USSR, Div. Chem. Sci., 1958, 1938), the authors noted the error of their previous results and from a reexamination of the reaction of trimethyl phosphite with phosgene arrived at results similar to those described in the present work.

The results we obtained in studying the reactions of full esters of phosphorous acid with phosgene were different from those described [6]. By the action of phosgene on triethyl phosphite we obtained the acid chloride (IV), which readily exchanged chlorine for an ethoxyl group to form the ester (V) when treated with ethyl alcohol in the presence of pyridine or sodium ethylate in an alcohol-ether solution. On the basis of data from investigation [6], we must have obtained the ethyl ester of diethylphosphonoformic acid (VI).

$$\underset{(VI)}{(C_2H_5O)_2\overset{\overset{\displaystyle O}{\|}}{P}—COOC_2H_5}$$
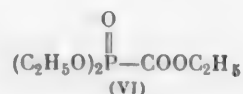
This ester was synthesized previously by A. E. Arbuzov and A. A. Dunin [7] by reacting triethyl phosphite with chlorocarbonic ester, but it differed in its properties from the product that we obtained. For a fuller characterization of (VI), we repeated its synthesis by the method in [7]. The constants of the products obtained are presented in Table 1.

TABLE 1

| Expt. No.	Product	Boiling point (pressure in mm)	$n^{20}D$	d^{20}_4
1	(V), obtained by the action of ethyl alcohol on the acid chloride (IV)	88-89° (8.5)	1.4060	1.0725
2	Ethyl ester of phosphonoformic acid (VI) (by Arbuzov's method)	124.5-125.5 (8.5)	1.4232	1.1272
3	Triethyl phosphate	91 (9)	1.4058	1.0726

From the data in Table 1, it is seen that the properties of product (V) are identical not with those of ethyl phosphonoformate (VI) but with those of triethyl phosphate, which was synthesized by the usual method of reacting ethyl alcohol with phosphoryl chloride. We also reacted the acid chloride (IV) with alcoholates of methyl and n-butyl alcohols and obtained the methyldiethyl and n-butyldiethyl esters of phosphoric acid, respectively. Their constants were identical with the constant reported in the literature for these esters and also the constants of the esters we obtained by reacting the same alcohols with diethylphosphoryl chloride.

To explain these results, one may postulate that either during the formation of the acid chloride by the action of phosgene on triethyl phosphite or in the formation of the esters from the acid chloride (I), the reaction proceed with elimination of the CO group. To test the first of these propositions, we reacted phosgene with the methyl, ethyl, butyl and isobutyl esters of phosphorous acid (method A) and synthesized some acid halides of dialkylphosphoric acids by the action of chlorine on appropriate dialkylphosphorous acids (method B). Table 2 shows the constants and the analysis data of the acid halides obtained by the two methods.

As is seen, the products obtained by methods A and B are completely identical in their properties and are the corresponding acid chlorides of the dialkylphosphoric acids. Conseqeuently, in all the cases we studied the reaction of phosgene with full esters of phosphorous acid proceeds with the elimination of the CO group by the equation:

$$(RO_3)P + COCl_2 \rightarrow (RO)_2\overset{\overset{\displaystyle O}{\|}}{P}—Cl + RCl + CO.$$
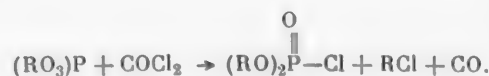
The error of Kabachnik and Rossiiskaya [6] apparently arose due to the inaccurate analytical data and specific gravity determination that they had available.

The reaction of dimethylphosphoryl chloride with trimethyl phosphite naturally formed not the ester of carbonyldiphosphinic acid, but, as was recently shown by Baudler and Griese [8], the anhydride of the acid

TABLE 2

Acid Chlorides of Dialkylphosphoric Acids

Formula	Method	B. p. (pressure in mm)	n_s^{20}	d_s^{20}	%P found	%P calc.	%C found	%C calc.
$(CH_3O)_2POCl$ {	A	64.5—65° (9)	1.4119	1.3396	21.46	21.45	25.16	24.57
	B	64.5—65 (9)	1.4119	1.3412	—	—	—	—
$(C_2H_5O)_2POCl$ {	A	78.5 (8)	1.4180	1.1979	17.68	17.97	20.33	20.6
	B	78 (7.5)	1.4171	1.1973	18.17	17.97	—	—
$(n-C_4H_9O)_2POCl$	A	120 (11)	1.4312	1.0760	13.38	13.89	—	—
$iso-C_4H_9O)_2POCl$	A	110—110.5 (8)	1.4268	1.0699	13.94	13.89	—	—

methyl ester of phosphoric acid and the acid ethyl ester of methylphosphinic acid, which they called an ester of iso-subphosphoric acid.

$$(CH_3O)_2P(=O)—Cl + (CH_3O)_3P \rightarrow (CH_3O)_2P(=O)—O—P(=O)\overset{CH_3}{\underset{OCH_3}{<}}$$
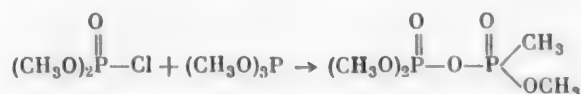
A similar ethyl ester was obtained by A. E. Arbuzov and B. A. Arbuzov [9] by isomerizing the acid ethyl ester of phosphoric acid and the acid ethyl ester of phosphorous acid with the aid of ethyl iodide.

Then, we studied the reaction of trimethyl phosphite and triethyl phosphite with the acid chloride of oxalic acid. In this case also, we obtained acid chlorides of dialkyl esters of phosphoric acid, but in lower yields than when phosgene was used. The reaction proceeded with the elimination of the two CO groups.

$$(RO_3)P + ClCO—COCl \rightarrow (RO)_2P(=O)Cl + 2CO + RCl$$
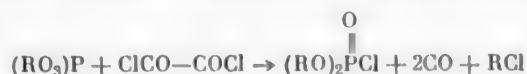
The reaction of triethyl phosphite with the acid chloride of maleic acid proceeded very vigorously and gave tarry products. Reactions in solvents also gave similar results.

EXPERIMENTAL

a) A stream of dry phosgene was passed through the phosphite in a round-bottomed flask fitted with a reflux condenser. The reaction mixture heated up and the alkyl chloride and carbon monoxide liberated during the reaction were carried away with the phosgene stream. In some cases the reaction mixtures were cooled with cold water. At the end of the reaction, the dissolved phosgene and alkyl chloride were pumped off with a water pump and the reaction mixtures vacuum distilled.

b) The phosphite was slowly added to liquid phosgene in a round-bottomed flask and cooled with a cooling mixture. When the phosphite had been added, the liquid was stirred for a further half an hour, then the volatile products pumped off and the residue vacuum distilled. The yields of dialkylchlorophosphates, obtained by the two methods, differed little from each other and were usually 60-70%.

Reaction of triethyl phosphite with oxalyl chloride. With cooling and continuous stirring, 40 g of triethyl phosphite was slowly added to 30 g of oxalyl chloride, dissolved in 100 ml of ether. When the phosphite had been added, the reaction mixture was heated on a water bath for 1 hour, the ether removed and the residue vacuum distilled. We obtained 12.7 g of diethyl chlorophosphate.

B. p. 78-79° (8 mm), n^{20}D 1.4178, d^{20}_4 1.1976, MR_D 36.19; calc. 35.89. Found %: P 17.70. $C_4H_{10}O_3PCl$. Calculated %: P 17.97.

A similar reaction with trimethyl phosphite yielded dimethyl chlorophosphate.

SUMMARY

It was shown that the reaction of full esters of phosphorous acid with phosgene and oxalyl chloride proceeded with elimination of carbon monoxide and yielded acid chlorides of dialkyl esters of phosphoric acid.

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ADDITION OF FULL ESTERS OF PHOSPHOROUS AND PHOSPHINOUS ACIDS TO CONJUGATED SYSTEMS

VII. TELOMERIZATION OF METHACRYLIC ACID WITH TRIALKYL PHOSPHITES

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In studying the combined action of α, β-unsaturated acids and alkyl halides with trialkyl phosphites [1, 2], we found that in some cases the reaction between them acquired the character of a telomerization. In continuing the investigation in this direction, we set out to find a more suitable catalyst for the telomerization reaction, to determine the factors affecting the course of this reaction and to study the structure of the telomers obtained. It was found that carefully purified (over sodium) triethyl phosphite could be also telomerized with methacrylic acid without a catalyst. The telomerization occurred both at room temperature and on heating. In this case the amount of telomer obtained was insignificant (Table 1, Experiment 13). If the same reaction was performed with methacrylic acid that had been kept for a long time unstabilized with hydroquinone, the reaction proceeded vigorously with considerable heat evolution and a high yield of telomer was obtained (Table 1, Experiment 12). Trialkyl phosphite, purified by simple distillation, was not telomerized with methacrylic acid freed from inhibitor immediately before the experiment.

In studying the reaction of β-lactones with trialkyl phosphites, McConnel and Coover [3] found that they were capable of telomerization with trialkyl phosphites in the presence of triethylamine and sodium methylate. It seemed interesting to us to determine how the telomerization of methacrylic acid and trialkyl phosphites proceeded in the presence of these catalysts. The experiments we performed showed that although sodium methylate and triethylamine produced telomerization of trialkyl phosphites with methacrylic acid, the yield of telomers was insignificant and experiments on telomerization were difficult to reproduce in this case (Table 1, Expts. 1 and 2). A further study of the telomerization in the presence of alkyl iodides showed that in this case the telomerization proceeded only with comparatively large amounts of the latter and not in the presence of catalytically small amounts (Table 1, Expt. 8). This fact and also previously described experiments on the combined action of alkyl halides and α,β-unsaturated acids on trialkyl phosphites [2] indicated that the alkyl halide not only initiated the reaction, but also participated in the formation of the telomer molecule.

Benzoyl peroxide was found to be the most suitable catalyst for the telomerization of trialkyl phosphites with methacrylic acid. The effect of the molar ratio of the starting components, the catalyst concentration and the phosphite radical on the molecular weight of the telomer was determined in a study of the telomerization in the presence of benzoyl peroxide. Telomers with various average molecular weights were obtained, depending on these factors (Table 1). The telomers obtained were white powders, which did not have a definite melting point and darkened and carbonized on heating. The telomers were insoluble in acetone, dioxane, ether, chloroform, benzene, carbon tetrachloride, nitrobenzene, toluene, cyclohexane, aniline and water. They dissolved in methyl and ethyl alcohols and acetic acid on heating. The molecular weight of the telomers was determined from the percentage phosphorus content and in some experiments, ebullioscopically in methyl alcohol. The results of our experiments are presented in Table 1. The experiments showed that with an increase in the concentration of methacrylic acid in the starting mixture, the molecular weight of the telomer increased. Thus, at a phosphite to acid ratio of 1 : 1, the average molecular weight of the telomer was 504, at ratio of 1 : 5, it was 752 and at a ratio of 1 : 10, it was 1410 (Table 1, Expts. 3-5). The molecular

weight also depended on the catalyst concentration; with an increase in the benzoyl peroxide concentration, the average molecular weight of the telomer increased (within the limits of the experiments carried out). Thus, in the telomerization of triethyl phosphite with methacrylic acid at a ratio of 1:5, the dependence on benzoyl peroxide concentration is expressed in the following way:

Concentration of benzoyl peroxide (in %)	Average molecular weight
1.1	2109
0.01	752
0.001	515

As is known, in the polymerization of acrylates an inverse relation is observed. Apparently, in the case of telomerization a decrease in the benzoyl peroxide concentration leads to an increase in the competing reactions of the Arbuzov rearrangement so that the chains are broken more rapidly and the intensity of telomerization decreases.

A study of the effect of the phosphite radical on the tendency for telomerization showed that the higher the radical, the less actively the phosphite underwent telomerization. While the telomerization with triethyl phosphite began at room temperature with a benzoyl peroxide concentration of 0.001% (in some cases, as indicated above, without catalyst also), telomerization with tripropyl phosphite required a benzoyl peroxide concentration of not less than 0.2% and with tributyl phosphite, not less than 0.4%.

Our experiments on the reproducibility of the results showed that under the same conditions, telomers with identical average molecular weights were obtained. Data from three experiments on the telomerization of triethyl phosphite with methacrylic acid at a starting reagent ratio of 1:5, a benzoyl peroxide concentration of 0.01% by weight and a temperature of 20° are given below:

Average molecular weight of telomer	Telomer yield (in %)
752	24.4
775	20.0
792	20.0

Attempts to telomerize acrylic acid with triethyl phosphite were unsuccessful; in this case the only reaction was an Arbuzov rearrangement.

As is known, the polymerization of acrylates proceeds by a 1,2-addition and the reaction of α, β-unsaturated acids with trialkyl phosphites, by a 1,4-conjugated system. Therefore, one may postulate two different structures for the telomers obtained.

$$(RO_2)P \underset{\underset{O}{\|}}{} [CH_2-\underset{\underset{COOH}{|}}{\overset{\overset{CH_3}{|}}{C}}-]_{n-1}CH_2-\underset{\underset{CH_3}{|}}{CH}-COOR; \qquad (RO)_2P\underset{\underset{O}{\|}}{}[CH_2-CH-\underset{\underset{CH_3}{|}}{COO}]_nR$$

(I)   (II)

By determining the number of carboxyl groups in several telomers, we were able to show that the telomers obtained had a structure corresponding to formula (I). By the action of sodium hydroxide solution, we prepared the sodium salt of the telomer, which was soluble in water and insoluble in ethyl and methyl alcohols.

On the basis of our previously published work and the newly obtained experimental data, it can be postulated that the telomerization proceeds by the scheme given below.

To convirm the postulated reaction mechanism, we studied the interaction of methacrylic acid, activated with benzoyl peroxide, with the intermediate of the Arbuzov reaarangement, obtained by the addition of triethyl phosphite to methacrylic acid (Table 1,Expt. 11). Here the telomerization proceeded more rapidly than in the case when the starting components were mixed directly under otherwise similar conditions (Table 1,Expt. 4).

The telomers from these two experiments were similar in molecular weight. The results obtained firstl confirmed the telomerization reaction scheme we postulated and, secondly, compelled us to assume that the P-O bond in the intermediate of the Arbuzov rearrangement had an ionic character.
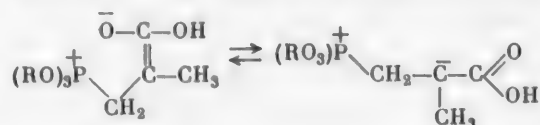
On being attacked by a methacrylic acid molecule, the intermediate product is converted into a carbonium ion and forms the beginning of the telomerization chain. If the intermediate product had a covalent structure, it could hardly act as the beginning of the telomer chain.
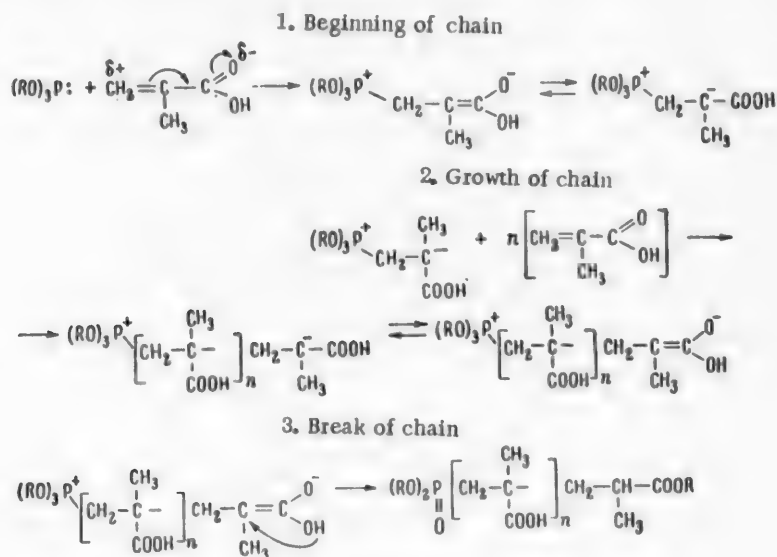
Scheme

1. Beginning of chain


2. Growth of chain

3. Break of chain

EXPERIMENTAL

Telomerization of methacrylic acid with triethyl phosphite (at a ratio of 5 : 1). 8.3 g of triethyl phosphite, 21.5 g of methacrylic acid and 0.03 g (0.01% by weight) of benzoyl peroxide were used for the reaction. The reaction was performed at room temperature. Turbidity appeared 30 minutes after the reagents had been mixed. A solid precipitate was formed after an hour. Three hours after the beginning of the reaction, the precipitate was filtered off, washed with ether and dried. The weight of telomer was 3.1 g. The filtrate again deposited a precipitate overnight and a further 0.7 g of telomer was isolated. The telomer obtained was a white, powdery product, which was insoluble in water, acetone, nitrobenzene, chloroform, cyclohexane, carbon tetrachloride and ether. It dissolved in ethyl and methyl alcohols and acetic acid on heating. All the other experiments on the telomerization of methacrylic acid with trialkyl phosphites were performed similarly.

The reaction of methacrylic acid in the presence of benzoyl peroxide with the intermediate addition product of methacrylic acid to triethyl phosphite. 4.15 g of triethyl phosphite and 2.15 g of methacrylic acid were used in the reaction. At the end of the reaction (the refractive index underwent no further change after 48 hours and a sample gave no rise in temperature with CuHal), a further 8.60 g of methacrylic acid and 0.001 g of benzoyl peroxide (0.01% by weight) were added. Five minutes after mixing turbidity appeared and the mixture heated up 10°. After 30 minutes a precipitate formed and this was filtered off, washed and dried. In properties and structure the telomer obtained was analogous to the telomer obtained by mixing the reagents directly.

TABLE 1

The Effect of Experimental Conditions on the Average Molecular Weight of the Telomers

$$(RO)_2P[CH_2-C(CH_3)-]_{n-1}CH_2-CHCOOR$$

with O ; $COOH$; CH_3
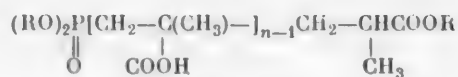
(Experiments at 20°)

Expt. No.	Starting reagents	Molar ratio of reagents	Catalyst	Percent of catalyst (by weight)	Phosphorous content (in %)	Average molecular wt. found from P	deter. ebullioscopically	Telomer yield (in %)
1*	$(C_2H_5O)_3P$ / $CH_2=C-COOH$ / CH_3	1 : 2	CH_3ONa	0.2	5.50	558	—	26.8
2	$(C_2H_5O)_3P$ / $CH_2=C-COOH$ / CH_3	1 : 2	$(C_2H_5)_3N$	0.4	5.40	582	—	25.2
3	$(C_2H_5O)_3P$ / $CH_2=C-COOH$ / CH_3	1 : 1	$(C_6H_5COO)_2$	0.01	6.10	504	—	47.3
4	$(C_2H_5O)_3P$ / $CH_2=C-COOH$ / CH_3	1 : 5	$(C_6H_5COO)_2$	0.01	3.90	752	665	24.4
5	$(C_2H_5O)_3P$ / $CH_2=C-COOH$ / CH_3	1 : 10	$(C_6H_5COO)_2$	0.01	2.40	1410	—	30.2
6	$(C_2H_5O)_3P$ / $CH_2=C-COOH$ / CH_3	1 : 5	$(C_6H_5COO)_2$	0.001	5.90	515	—	14.3
7	$(C_2H_5O)_3P$ / $CH_2=C-COOH$ / CH_3	1 : 5	$(C_6H_5COO)_2$	0.1	1.34	2109	—	89.2
8	$(C_2H_5O)_3P$ / $CH_2=C\ COOH$ / CH_3	1 : 5	iso-$C_5H_{11}I$	0.5 mole per mole of phosphite	3.56	854	—	18.9
9	$(C_2H_7O)_3P$ / $CH_2=C-COOH$ / CH_3	1 : 5	$(C_6H_5COO)_2$	0.2	3.40	930	855	34.5
10	$(C_2H_5O)_3P$ / $CH_2=C-COOH$ / CH_3	1 : 5	$(C_6H_5COO)_2$	0.4	1.38	2279	—	35.3
11	$-O-C=O$ + CH_3 / $(C_2H_5O)_3P$ $CHCH_3$ / CH_3 / $CH_2=C-COOH$ / CH_3	1 : 4	$(C_6H_5COO)_2$	0.01	4.60	680	—	51.2
12	$(C_2H_5O)_3P$ / $CH_2=C-COOH$ / CH_3	1 : 5	Without catalyst	—	2.57	1205	—	52.1
13	$(C_2H_5O)_3P$ / $CH_2=C-COOH$ / CH_3	1 : 5	Without catalyst	—	5.10	608	—	6.3

*Methacrylic acid, which had been without stabilizer for a long time was used in the reaction.

**In the presence of carefully purified triethyl phosphite.

TABLE 2

Expt. No.	Average molecular wt. of telomer	No. of carboxyl groups, corresponding to formula (I)	Sample of telomer (in g)	Titer of alkali	Alkali consumed in titration (in ml)	Am't of alkali required in theoretically
1	811	7	0.1462	0.0083	8.8	8.0
2	775	6	0.1590	0.0088	7.0	6.1
3	1371	13	0.1944	0.0083	8.6	8.0

Determination of the number of carboxyl groups in telomers. The number of carboxyl groups was determined in a solution in ethyl alcohol, previously titrated to a neutral reaction in the presence of phenolphthalein. An alcohol solution of NaOH was used for the titration. Data from the experiments are presented in Table 2.

SUMMARY

1. A study was made of the telomerization of trialkyl phosphites with methacrylic acid in the presence of various catalysts.

2. The effect of various factors on the molecular weight of the telomers obtained was determined.

3. A study was made of the structure of the telomers and a reaction scheme put forward for the telomerization of methacrylic acid with trialkyl phosphites.

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# SYNTHESIS OF BIOLOGICALLY INTERESTING THIAZOLIDONE DERIVATIVES

X. SYNTHESIS AND PROPERTIES OF 3-METHYLRHODANINE AND ITS DERIVATIVES

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3-Methylrhodanine, prepared by condensation of methyl mustard oil with thioglycolic acid in aqueous alcohol solution [1] has found application in the preparation of photosensitizers [2]. The preparation is of biological interest as a fungicide [3]. The condensation of 3-methylrhondanine with aromatic aldehydes [1] leads to the formation of 5-arylidene derivatives.

Carrying out the synthesis by Andreasch's method [1] involves certain difficulties due to the ready oxidizibility of thioglycolic acid. For the preparation of 3-methylrhodanine and its condensation products with aldehydes, we used a reaction which we proposed [4] and which consists of the condensation of mustard oils with thiocyanoacetates, that are readily accessibile and stable substances.
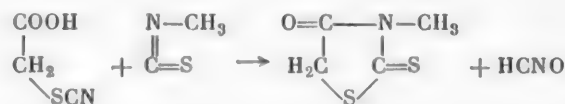
A mixture of sodium and potassium salts of thiocyanoacetic acid in the presence of glacial acetic acid and lead acetate was used in the condensation. The simultaneous introduction of aromatic aldehydes or furfural into the condensation reaction made it possible to obtain good yields (38-85%) of the 5-substituted 3-methylrhodanines in one stage. In this way we obtained 3-methylrhodanine and its benzylidene-, cinnamylidene-, m- and p-nitrobenzylidene-, p-anisylidene- o-carboxybenzylidene-, salicylidene- and furfurylidene derivatives.

3-Methylrhodanine is an unstable substance, which is hydrolyzed in an alkaine medium (solutions of NaOH and even NH_4OH), as indicated by a positive nitroprusside reaction. The introduction of an arylidene group into position 5 stabilizes the molecule, so that the 5-arylidene derivatives are only hydrolyzed by boiling with NaOH solutions. This gives Na_2S (a positive reaction with lead acetate and sodium nitroprusside) and salts of the thioketo acid $ArCH_2CSCOONa$ (positive reaction with $FeCl_3$ in an ammoniacal medium [5]).
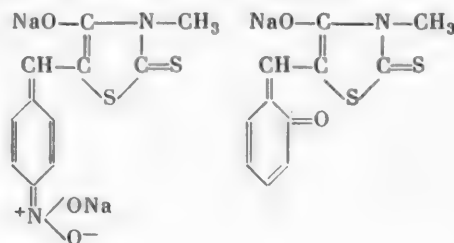
3-Methyl-5-salicylidenerhodanine and 3-methyl-5-p-nitrobenzylidenerhodanine dissolved in solution of NaOH or NH$_4$OH with the formation of intense red or orange solutions, respectively, and this may be explained by the formation of salts containing the ortho- or para-quinonoid grouping. The other arylidene derivatives of 3-methylrhodanine did not dissolve in NaOH solutions in the cold.
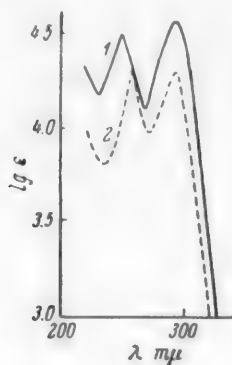

Fig. 1. Ultraviolet absorption spectrum curves: 1) rhodanine, 2) methylrhodanine.
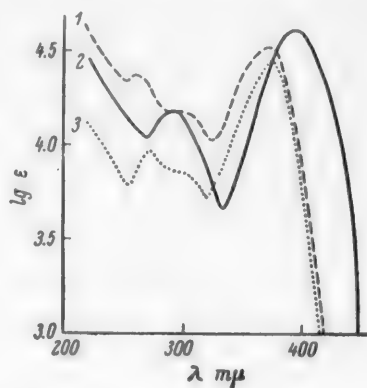
Fig. 2. Ultraviolet absorption spectrum curves: 1) 5-benzylidenerhodanine, 2) 3-methyl-5-anisylidenerhodanine, 3) 3-methyl-5-benzylidenerhodanine.

The introduction of a methyl group into position 3 of the rhodanine molecule does not displace the main maxima and minima of the ultraviolet absorption spectra and only reduces their intensities strongly (Fig. 1 and 2) in the short-wave region of the spectrum. The first absorption maximum of rhodanine and its 3-methyl derivatives (~255 mμ) is displaced toward longer wavelengths (260-278 mμ) when an arylidene substituent is introduced into position 5. The second maximum (~295 mμ) is thus changed into an inflection, except for the case of the anisylidene and the cinnamylidene derivatives. The introduction of arylidene substituents produces a new characteristic maximum in the region of 365-404 mμ. In connection with this, the long-wave edge of
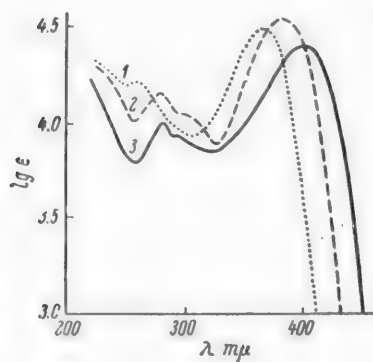
Fig. 3. Ultraviolet absorption spectrum curves: 1) 3-methyl-5-m-nitrobenzylidenerhodanine, 2) 3-methyl-5-p-nitrobenzylidenerhodanine, 3) 3-methyl-5-salicylidenerhodanine.
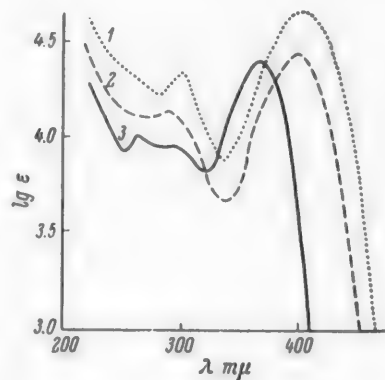
Fig. 4. Ultraviolet absorption spectrum curves: 1) 3-methyl-5-cinnamylidenerhodanine; 2) 3-methyl-5-furfurylidenerhodanine, 3) 3-methyl-5-o-carboxybenzylidenerhodanine.

the absorption curves at ε equals 1000 is displaced from ~320 mμ to the region of 410-465 mμ (Figs. 3 and 4). 3-Methyl-5-furfurylidenerhodanine behaves similarly to the arylidene derivatives. We should also note that the absorption spectra of the p-nitro derivative are displaced toward longer wavelengths in comparison with the spectra of the m-nitro derivative.

Investigations carried out in the histology department of the L'vov Medical Institute (A. P. Dyban, et al.) showed that the 3-methylrhodanine and its derivatives that we synthesized had an antithyroid acitivity.

EXPERIMENTAL

0.02 mole of methyl mustard oil, 3.8 g of a mixture of sodium and potassium thiocyanoacetates (corresponding to 0.02 mole of thiocyanoacetic acid), 15 ml of glacial acetic acid and 1.0 g of lead acetate were heated together in a flask with a reflux condenser for 15-60 minutes on a boiling water bath. The condensation proceeded vigorously with the evolution of carbon dioxide as a decomposition product of HCNO. When the evolution of CO_2 had ceased, the mixture was diluted with water. The condensation product was filtered off, washed with water and recrystallized from alcohol. We obtained 3-methylrhodanine with m. p. 75-76° in 41% yield.

When 0.02 mole of aldehyde was introduced into the condensation reaction simultaneously, we likewise obtained in one stage the 5-arylidene derivatives, whose melting points were identical with or a few degrees higher than those reported in the literature [1]. The substances that we synthesized for the first time are presented in the table.

Name of preparation	Yield (in %)	Melting point	N analysis (in %)	
			calc.	found
3-Methyl-5-salicylidenerhodanine	64	134-135°	5.58	5.86
3-Methyl-5-furfurylidenerhodanine	45	138-139°	6.22	6.56
3-Methyl-5-o-carboxybenzylidenerhodanine	38	227-228°	5.02	5.35

The spectrophotometric investigations were performed on a quartz SF-4 spectrophotometer. The light source was a VSFU-3 low voltage arc hydrogen lamp. The solutions of the substances investigated were at a concentration of ~1 mg/100 ml of ethyl alcohol.

SUMMARY

1. A description is given of a simple and convenient synthesis of 3-methylrhodanine and its 5-arylidene derivatives, based on the condensation of salts of thiocyanoacetic acid with methyl mustard oil in the presence of acetic acid, lead acetate and aldehydes.

2. The introduction of arylidene substituents into the 3-methylrhodanine molecule produces a characteristic absorption maximum in the region of 365-404 mμ. Simultaneously, the long-wave edge of the absorption curves at ϵ equals 1000 is displaced by 90-145 mμ toward longer wavelengths.

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*Original Russian pagination. See C.B. Translation.

DYES WITH ANTIPYRINE NUCLEI

VI. DYES WITH ONE ANTIPYRINE NUCLEUS

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Dyes whose structures contain only one antipyrine ring may be prepared by various methods. Thus, for example, heating antipyrine with Michler's ketone in the presence of phosphorus trichloride gives dye (I), whose ion corresponds to the structure (I).
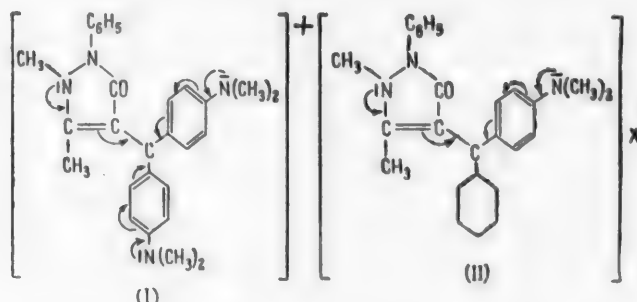
Dye (I) imparts a blue color to tannated cotton and a violet color to wool fiber. The absorption spectrum of this dye (Fig. 1) has two clearly expressed maxima, with one of the maxima close to the position of the maximum of the Antipyrine orange absorption spectrum and the other close to the position of the maximum of the Crystal violet absorption spectrum. When treated with alkali, dye (I) is converted into bis-(p-dimethylaminophenyl)-antipyrylcarbinol, which, in its turn, is converted into the dye on acidification.

The other dye (II), which contains one antipyrine ring, was synthesized starting from antipyryl phenyl ketone and dimethylaniline. It absorption spectrum is illustrated in Fig. 1.

We also attempted to prepare dye (II) by reacting 4-dimethylaminobenzophenone with antipyrine in the presence of phosphorus trichloride. However, from this we obtained only traces of dye (II) and the reaction mixture yielded diantipyrylmethane, which in all probability was formed as a result of extensive decomposition of 4-dimethylaminobenzophenone under these conditions.

Dye (II) is an unsymmetrical dye and contains groupings characteristic of both Antipyrine orange and Malachite green. It is known that the absorption maxima of unsymmetrical cyanine dyes are close to the arithmetic mean of the absorption maxima of the corresponding symmetrical dyes [1]. Comparison of the position of the absorption maximum of the unsymmetrical dye (II) (545 mμ) with the positions of the absorption maxima of Malachite green (616 mμ) and Antipyrine orange (480 mμ) shows that dye (II) has an absorption maximum whose position is also close to the arithmetic mean of the absorption maxima of Malachite green and Antipyrine orange.

Like other triarylmethane dyes, the newly synthesized dyes are hydrolyzed in aqueous solutions. The hydrolysis constants of the dyes, found by a colorimetric method, are given in Table 1. For comparison, the hydrolysis constants of Antipyrine orange and Malachite green are given in the same table.

An examination of Table 1 shows that the unsymmetrical dye (II) has a lower hydrolysis constant than the symmetrical dyes Antipyrine orange and Malachite green. Since the stability of conjugate carbonium ions to hydrolysis is in direct proportion to the magnitude of the conjugation effect, this indicates that the conjugated effect is greater in the unsymmetrical dye (II) than in the symmetrical Antipyrine orange and Malachite green.
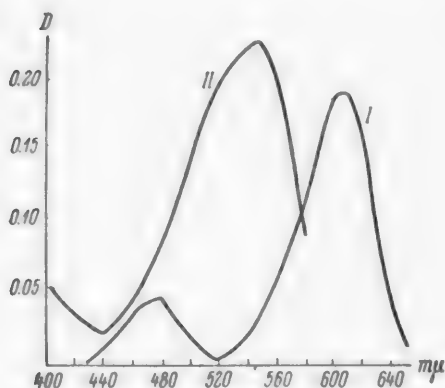
Absorption curves of dyes (I) and (II).

TABLE 1

Hydrolysis Constants of Triarylmethane Dyes

Dye	K_H
Dye (I)	$1.55 \cdot 10^{-10}$
Dye (II)	$1.98 \cdot 10^{-8}$
Malachite green	$1.26 \cdot 10^{-7}$
Antipyrine orange	$2.50 \cdot 10^{-7}$

Thus, in this case, we encounter an extremely unusual form of the mutual effect, caused by the unsymmetrical structure of the sections of the molecule. This form of mutual effect requires further study.

EXPERIMENTAL

Bis(p-dimethylaminophenyl)-antipyrylcarbinol. 12.0 g of Michler's ketone and 8.4 g of antipyrine were dissolved in 150 ml of chlorobenzene and heated on a water bath in a flask fitted with a reflux condenser and a stirrer. Over a period of 1 hour 12.0 g of phosphorus trichloride was added to the reaction mixture dropwise. After being heated for 5 hours, the reaction mixture was cooled and 100 ml of water carefully added. The intensely colored aqueous layer was separated from the chlorobenzene layer and made alkaline with 40% sodium hydroxide solution. The dark tarry precipitate was filtered off and treated with 5% acetic acid solution (300 ml) with heating. The acetic acid solution was separated from the insoluble part of the precipitate (unreacted Michler's ketone) and slowly neutralized at 10-15° with 5% sodium hydroxide solution. The precipitate was filtered off and dried at 80°. We obtained 5.0 g. After two recrystallizations from a mixture of benzene and benzine (1:1), the product melted at 197-198°.

Found %: N 12.54. $C_{28}H_{32}O_2N_4$. Calculated %: N 12.27.

Picrate of bis(p-dimethylaminophenyl)-antipyrylcarbinol. To a hot solution of 5 g of bis (p-dimethylaminophenyl)-antipyrylcarbinol in 50 ml of alcohol was added a hot solution of 2.4 g of picric acid in 20 ml of alcohol. The picrate of the dye precipitated and after recrystallization from alcohol, it had m. p. 196-198°.

Found %: C 61.15; 60.98; H 5.70, 5.55; N 14.43. Titanium number 281.* $C_{28}H_{31}ON_4 \cdot C_6H_2O_7N_3$ Calculated %: C 61.16; H 4.98; N 14.69. Titanium number 299.

p-Dimethylaminophenyl-phenyl-antipyrylcarbinol. 2.0 g of antipyryl phenyl ketone [2] and 2.0 g of phosphorus trichloride were heated in a flask fitted with a reflux condenser until a homogeneous, dark red, viscous mass was obtained. Then 4.0 g of dimethylaniline was added and the mixture heated for 4 hours on a water bath. The reaction mixture was cooled, broken up with 50 ml of water, made alkaline and the dimethylaniline removed by steam distillation. The precipitate formed was filtered off and treated with 50 ml of 0.1 N hydrochloric acid. The hydrochloric acid filtrate was made alkaline with sodium hydroxide solution. The precipitate was filtered off and dried. We obtained 0.6 g of a substance with m. p. 155-157°. This compound was recrystallized from a mixture of benzene and benzine (1:2) and then dissolved in 50 ml of ether. When the ether solution was evaporated to a volume of 20 ml, it deposited an almost colorless product with m.p. 214-215°.

*The picrates of the dyes were titrated titanometrically in 60% aqueous alcohol.

Found %: N 10.0, 10.52. M 422 (potentiometric titration). $C_{26}H_{27}O_2N_3$. Calculated %: N 10.17. M 413.

Picrate of p-dimethylaminophenyl-phenyl-antipyrylcarbinol. To a hot solution of 0.1 g of carbinol in 5 ml of alcohol was added a solution of 0.05 g of picric acid in 5 ml of alcohol. The precipitate was recrystallized from alcohol. The picrate did not have a sharp melting point.

Found %: N 13.58, 13.80. Titanium number 324. $C_{26}H_{26}ON_3 \cdot C_6H_2O_7N_3$. Calculated %: N 13.50. Titanium number 320.

Condensation of antipyrine with p-dimethylaminobenzophenone. Over a period of 1 hour, 4.0 g of phosphorus trichloride was added dropwise to a solution of 4.5 g of p-dimethylaminobenzophenone and 3.7 g of antipyrine in 100 ml of chlorobenzene at 80-90°. After 3 hours heating, the mixture was cooled and then mixed with 100 ml of water. The aqueous layer was separated from the chlorobenzene and made alkaline with sodium hydroxide solution. The precipitate formed was filtered off and dried. After three recrystallizations from benzene, the product had m. p. 177-178°. A mixed sample of the compound obtained and diantipyrylmethane [3], which has m. p. 179°, did not have a depressed melting point. The benzene mother liquors yielded a small amount of a dye, whose absorption spectrum was identical with that of the dye obtained from p-dimethylaminophenyl-phenyl-antipyrylcarbinol.

TABLE 2

Optical Density Change of Dye Solutions in Relation of pH Value

Name of compound	Am't of dye solution (in ml)	λ (in mμ)	pH	D	α	pK_g
Bis(p-dimethylaminophenyl)-anti-pyrylcarbinol	0.40	607	7.4	1.65	(1)	—
			8.88	1.47	0.895	9.79
			9.75	0.88	0.534	9.87
			9.90	0.74	0.448	9.81
Picrate of p-dimethylaminophenyl-phenyl-antipyrylcarbinol	0.20	545	3.8	0.620	(1)	—
			7.35	0.400	0.645	7.64
			8.11	0.200	0.323	7.79
			8.44	0.098	0.158	7.71

Hydrolysis constant determination on dyes. $5 \cdot 10^{-5}$ mole of carbinol or picrate was dissolved in 50 ml of acetone. Similar amounts of this solution were added to 25.0 ml portions of several buffer solutions with different pH values. When equilibrium had been established in the solution, the optical density was measured on a Konig — Martins spectrophotometer at the wavelengths given below. The layer thickness of the solution examined was 20 mm and the temperature $17 \pm 1°$. The data obtained is presented in Table 2.

SUMMARY

1. The reaction of Michler's ketone with antipyrine and antipyryl phenyl ketone with dimethyl aniline gave triarylmethane dyes, containing one antipyrine ring.

2. The unsymmetrical dye formed from antipyryl phenyl ketone and dimethylaniline had a greater stability toward hydrolysis than the corresponding symmetrical dyes, Malachite green and Antipyrine orange.

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STUDIES IN ORGANIC INSECTOFUNGICIDES

XXXVIII. REACTION OF PHOSPHORUS THIOTRICHLORIDE AND ALKYLDICHLORO-THIOPHOSPHATES WITH ALCOHOLS

N. N. Mel'nikov, Ya. A. Mandel'baum and P. G. Zaks

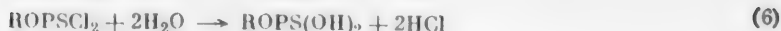Scientific Institute of Fertilizers and Insectofungicides

In recent years, dialkylchlorothiophosphates, which are used for the production of the most important contact and systemic insecticides, have acquired quite a considerable importance. In most cases dialkylchlorothiophosphates are obtained by the action of phosphorus thiotrichloride or alkyldichlorothiophosphates on alcoholates of various metals [1-5] or on alcohols in the presence of various bases [6-10]. Until very recently it was impossible to obtaine these dialkylchlorothiophosphates or trialkylthiophosphates by the reactions of alcohols with phosphorus thiotrichloride or alkyldichlorothiophosphates in the absence of substances which combine with the hydrogen chloride liberated during these reactions. Thus, for example, the reaction of phosphorus thiotrichloride with alcohols yielded alkyldichlorothiophosphates as the main reaction products. Heating phosphorus thiotrichloride with excess alcohol (1 mole of phosphorus thiotrichloride and 2 moles of alcohol) gave the corresponding alkyl halide and alkylthiophosphoric acid, together with the alkyldichlorothiophosphate [11]. The reaction of alkyldichlorothiophosphate with alcohol proceeded in exactly the same way. These reactions may be represented by the following general schemes, (1) and (2).

$$PSCl_3 + 3ROH \longrightarrow ROPS(OH)_2 + 2RCl \tag{1}$$

$$ROPSCl_2 + 2ROH \longrightarrow ROPS(OH)_2 + 2RCl \tag{2}$$
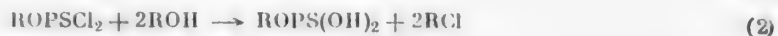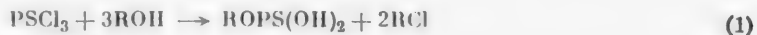
At the same time, from a large amount of experimental data on the reactions of alcohols with the acid chlorides of various organic and inorganic acids, one would expect that dialkylchlorothiophosphates would also be formed by reaction of phosphorus thiotrichloride and alkyldichlorothiophosphates with alcohols.

In connection with this, we undertook to study the reactions of phosphorus thiotrichloride and alkyldichlorothiophosphates with alcohols under various conditions. The experiments showed that different products could be obtained with different reaction conditions and ratios of the reacting materials. Thus, the reaction of 2 moles of ethyl alcohol with 1 mole of phosphorus thiotrichloride at 40-50° gave a 45-50% yield of ethyldichlorothiophosphate and about 20% of ethylthiophosphoric acid, which agrees completely with the observations of P. S. Pishchemuka [11]. The reaction of 1 mole of phosphorus thiotrichloride with 4 moles of ethyl alcohol at 50-60° formed a mixture of esters in 46-48% yield, which contained 80% of ethyldichlorothiophosphate and 20% of diethylchlorothiophosphate, while more prolonged heating on a boiling water bath made it possible to obtain almost pure diethylchlorothiophosphate. However, in this case its yield did not exceed 10%. Under the given conditions, ethylthiophosphoric acid and ethyl chloride were formed together with esters of chlorothiophosphoric acids.

The experimental results presented give direct indications of the direction of the reaction of phosphorus trichloride with alcohols. The reactions of phosphorus thiotrichloride with alcohols and their sequence may be represented by schemes (3-7).

$$PSCl_3 + ROH \longrightarrow ROPSCl_2 + HCl \tag{3}$$

$$ROH + HCl \longrightarrow RCl + H_2O \tag{4}$$

$$ROPSCl_2 + ROH \longrightarrow (RO)_2PSCl + HCl \tag{5}$$

$$ROPSCl_2 + 2H_2O \longrightarrow ROPS(OH)_2 + 2HCl \tag{6}$$

$$(RO)_2PSCl + H_2O \longrightarrow (RO)_2PSOH + HCl \tag{7}$$

On the basis of the schemes presented for the reaction of phosphorus thiotrichloride with alcohols, one may arrive at the conclusion that with sufficient dilution of the reaction medium with alcohol to decrease the rate of alkyl chloride and water formation, it would be possible to obtain   more or less satisfactory yields of dialkylchlorothiophosphates. This conclusion was confirmed completely experimentally. The dialkylchloro-thiophosphates obtained in this way are listed in Table 1.

Considerably better yields of dialkylchlorothiophosphates were obtained by the reaction of alcohols with alkyldichlorothiophosphates, which is quite understandable since the concentration of hydrogen chloride in solution is less in the latter case and consequently, side processes which give alkylthiophosphoric acids occur to a lesser extent.

The highest yields of dialkylchlorothiophosphates were obtained by the reaction of different alkyldichloro-thiophosphates with methyl alcohol, which is explained by the high activity of the hydroxyl hydrogen in methyl alcohol in comparison with other alcohols [12]. The dialkylchlorothiophosphates we obtained in this way are listed in Table 2

The reactions of methyl alcohol with phosphorus thiotrichloride or alkyldichlorothiophosphate made it possible to obtain even the corresponding trialkylthiophosphates, though in relatively low yields. The compounds we obtained by this method are listed in Table 3.

TABLE 1

Preparation of Dialkylchlorothiophosphates from Phosphorus Thiotrichloride and Alcohols

Formula of dialkylchloro-thiophosphate obtained	No. of moles of alcohol/ mole of $PSCl_3$ taken for the reaction	Duration of reaction (in hr)	Yield (in %)	Constants of compound obtained *		
				boiling point (pressure in mm)	d_4^{20}	n_D^{20}
$(CH_3O)_2PSCl$	10	3	53	65—66° (16) [66(16)]	1.3351 (1.3414)	1.4834 —
$(C_2H_5O)_2PSCl$	60	24	34	96—97(25) [96—99(25)]	1.2019 (1.2017)	1.4670 (1.4678)
$(C_3H_7O)_2PSCl$	60	27	46	110(17) [109—112(17)]	1.1646 (1.1644)	1.4670 (1.4677)
$(C_4H_9O)_2PSCl$	60	29	48	128(10) [141—142(15)]	1.0694 (1.0696)	1.4660 (1.4610)

* The constants according to literature data are given in brackets.

The experimental data presented show quite conclusively that phosphorus thiotrichloride and alkyldi-chlorothiophosphates behave as typical acid chlorides and react exactly like the acid halides of other inorganic and organic acids.

EXPERIMENTAL

Reaction of phosphorus thiotrichloride with alcohols. In order to prepare dialkylchlorothiophosphates from the appropriate alcohol and phosphorus thiotrichloride, phosphorus thiotrichloride was placed in a flask fitted with a reflux condenser and a mechanical stirrer and the alcohol gradually added to it with vigorous stirring and cooling (15-20°). When the required amount of alcohol had been added, the reaction mixture was kept at a definite temperature for a certain time. The alcohol was then washed out with water (in the case of water-soluble alcohols) or removed in vacuum and the dialkylchlorothiophosphate fractionated in vacuum.   The

T A B L E   2

Preparation of Dialkylchlorothiophosphates from Alkyldichlorothiophosphates and Alcohols

Formula of di-alkylchloro-thiophosphate obtained	Moles of alcohol/mole of ROPSCl$_2$ taken for the reaction	Duration of reac-tion (in hours)	Temper-ature	Yield (in %)	Constants of compounds obtained		
					boiling point (pressure in mm)	$d\%$	n^{20}_D
(CH$_3$O)$_2$PSCl *	10	6	5—10°	71	56—57° (10)	1.3351	1.4834
(C$_2$H$_5$O)$_2$PSCl	40	24	20—30	61	95 (20)	1.2020	1.4680
(C$_3$H$_7$O)$_2$PSCl	40	24	20—30	63	109—111 (17)	1.1648	1.4650
(C$_4$H$_9$O)$_2$PSCl	40	25	25	60	140—142 (15)	1.0695	1.4601
CH$_3$O\C$_2$H$_5$O PSCl ***	15	4	20—25	81	80—81 (17)	1.2506 **	1.4740
CH$_3$O\n-C$_3$H$_7$O PSCl	10	1.5	30—35	65	107—110 (25)	1.1852 **	1.4650
CH$_3$O\n-C$_4$H$_9$O PSCl	11	1.5	30	77	45—47 (0.3)	1.1830 **	1.4765
CH$_3$O\iso-C$_4$H$_9$O PSCl	12	2.0	30—35	90	110—114 (22)	1.1364 **	1.4600
CH$_3$O\iso-C$_5$H$_{11}$O PSCl	10	3.5	30	92	138—140 (32)	1.1261 **	1.4672

*All the esters of chlorothiophosphoric acid presented in the table were analyzed for phosphorus content.

**d^{20}_4.

***In a report published previously [8], we gave the constants of this compound incorrectly and we apologize for this.

T A B L E   3

Synthesis of Trialkylthiophosphates from Methanol and Alkyldichlorothiophosphates or PSCl$_3$

Formula of tri-alkylthiophos-phate obtained	Moles of alcohol/mole of ROPSCl$_2$ taken in the reaction	Duration of reac-tion (in hours)	Tem-pera-ture	Yield (in %)	Constants of compounds obtained		
					boiling point (pressure in mm)	d^{20}_4	n^{20}_D
(CH$_3$O)$_3$PS *	60	48	20°	6	72—74° (13)	1.2192	1.4599
(CH$_3$O)$_3$PS **	40	26	20	32	81 (20)	1.2189	1.4600
(CH$_3$O)$_3$PS ***	20	24	20	56	81—83 (20)	1.2191	1.4597
(CH$_3$O)$_2$PSOC$_2$H$_5$	20	24	20—30	46	96 (25)	1.1507	1.4520
(CH$_3$O)$_2$PSOC$_3$H$_7$	20	24	20—30	73	104—105 (22)	1.1203	1.4571
(CH$_3$O)$_2$PSOC$_4$H$_9$	20	25	20—30	30	114 (20)	1.0941	1.4560

*From methanol and phosphorus thiotrichloride.

**From methanol and methyldichlorothiophosphate.

***From methanol and dimethylchlorothiophosphate.

compounds we obtained in this way and their preparation conditions are presented in Table 1. We should note that if the given conditions for the preparation of dialkylchlorothiophates were not observed, even with small deviations there was a considerable change in the yield.

To prepare trialkylthiophosphates, the reaction of phosphorus thiotrichloride with alcohols was performed under similar conditions, but with different reagent ratios and longer reaction times. Of all the alcohols studied, only methyl alcohol and phosphorus thiotrichloride yielded a trialkylthiophosphate – trimethylthiophosphate. With other alcohols, the reaction did not go to trialkylthiophosphates under the conditions studied. The conditions for preparing trimethylthiophosphate are given in Table 3.

Reaction of alcohols with alkyldichlorothiophosphates. Under the conditions described above, the alkyl-dichlorothiophosphate was mixed with the appropriate alcohol in ratios selected experimentally and kept at the given temperature for a definite time. Afterward the reaction mixture was cooled and washed with water. The dialkylchlorothiophosphate was then fractionated in vacuum. The compounds we obtained by this method and their synthesis conditions are presented in Table 2.

By the reaction of methyl alcohol with various alkyldichlorothiophosphates and dimethylchlorothiophosphate, we synthesized the corresponding trialkylthiophosphates, whose properties and preparation conditions are given in Table 3.

SUMMARY

The reactions of phosphorus thiotrichloride and alkyldichlorothiophosphates were studied. It was shown that phosphorus thiotrichloride and alkyldichlorothiophosphates react with alcohols like normal acid chlorides and that the alkylthiophosphoric acids obtained as side products were formed as a result of hydrolysis of the starting and final esters of chlorothiophosphoric acid.

A new method for the preparation of dialkylchlorothiophosphates by the reaction of alcohols with phosphorus thiotrichloride or alkyldichlorothiophosphates was developed. In most cases, the dialkylchlorothiophosphates were obtained in satisfactory or good yields by this method.

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STUDIES IN ORGANIC INSECTOFUNGICIDES

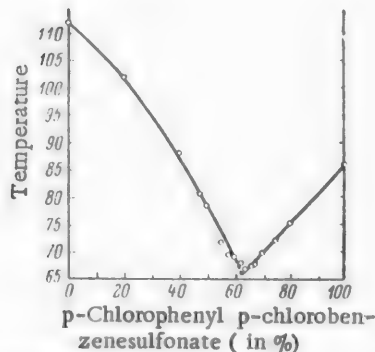## XXXIX. FUSION DIAGRAM OF THE BINARY SYSTEM OF o- AND p-CHLOROPHENYL p-CHLOROBENZENESULFONATES AND A CRYOSCOPIC METHOD OF DETERMINING p-CHLOROPHENYL p-CHLOROBENZENESULFONATE

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One of the long acting acaricides, which has found wide application in the fight against plant pests, is p-chlorophenyl p-chlorobenzenesulfonate (I), which is known under the technical names of Ester Sulfonate, Ovotran, etc. [1, 2]. The preparation put out industrially usually contains as impurities o-chlorophenyl p-chlorobenzenesulfonate (II), 2,4-dichlorophenyl p-chlorobenzenesulfonate (III) and small amounts of phenyl p-chlorobenzenesulfonate, which have a considerably lower acaricide activity, and due to this it is necessary to use higher concentrations of the technical preparation, which in some cases may constitute a danger to the plants treated. However, since the technical preparation consists of a mixture of isomers and related compounds, the determination of the active substance is extremely difficult. Up to the present there have been no methods for determining (I) in a mixture with the compounds listed above and all the analysis methods recommended allow the determination of either the total of all the substances or, in the best case, the total of the isomers [3]. We attempted to devise an analysis of this mixture by using the physicochemical properties of the substance and, in particular, the cryoscopic constant (I), especially as the cryoscopic method is used successfully for analyzing Lindan and certain DDT preparations [4-6]. Pure γ-hexachlorocyclohexane is used as the solvent in the analysis of Lindan.

To study the applicability of the cryoscopic method in analyzing (I), we first studied the fusion diagram of the binary system of p-chlorophenyl p-chlorobenzenesulfonate – o-chlorophenyl p-chlorobenzenesulfonate and determined the cryoscopic constant of (I), which was found to be 13.40 (from ten determinations, see Table 1). The fusion diagram of the binary system of p-chlorophenyl p-chlorobenzenesulfonate – o-chlorophenyl p-chlorobenzenesulfonate is given in the figure.

As a result of the experiments, it was established that the cryoscopic method is suitable for analyzing the mixture of isomers and related compounds present in the technical preparation of (I). The error in determining the content of (I) did not exceed 1%. To illustrate this method of determining (I), data are presented in Table 2 on the analysis of the ternary mixture of p-chlorophenyl p-chlorobenzenesulfonate, o-chlorophenyl p-chlorobenzenesulfonate and 2,4-dichlorophenyl p-chlorobenzenesulfonate.

Fusion diagram of the p- and o-chlorophenyl p-chlorobenzenesulfonate system.

EXPERIMENTAL

Starting materials. The p-chlorophenyl, o-chlorophenyl and 2,4-dichlorophenyl, p-chlorobenzenesulfonates required for the work were synthesized by reacting the appropriate phenolates with p-chlorobenzenesulfonyl chlorides.

TABLE 1

Solidification Point of Mixtures of o- and p-Chlorophenyl p-Chlorobenzenesulfonates

Content of isomers in mixture (in %)		Solidification point of mixture	Δt	Cryoscopic constant
para	ortho			
100	0	85.7°		
95	5.0	83.6	2.1	13.82
94	6.0	82.9	2.8	13.26
93.24	6.76	82.6	3.1	12.96
92.60	7.40	82.1	3.6	13.64
92.00	8.00	82.0	3.7	13.84
91.00	9.00	81.3	4.4	13.47
90.91	9.09	81.2	4.5	13.64
90.00	10.00	80.9	4.8	13.11
89.60	10.40	80.6	5.1	13.33
88.00	12.00	79.9	5.8	12.98
80.00	20.00	75.1	10.6	
75.00	25.00	72.1	13.6	
70.00	30.00	69.8	15.9	
67.00	33.00	67.8	17.9	
64.00	36.00	66.8	18.9	
60.900	40.00	69.2		
57.6	42.4	69.5		
55.00	45.00	71.8		
50.00	50.00	78.7		
48.00	52.00	80.8		
40.00	60.00	88.1		
20.00	80.00	101.8		
0	100	111.7		

These substances were purified by several recrystallizations from benzene and ethyl alcohol.

The preparations used for this work had the following constants: p-chlorophenyl p-chlorobenzenesulfonate, m. p. 86.5°, o-chlorophenyl p-chlorobenzenesulfonate, m. p. 111.5°, and 2,4-dichlorophenyl p-chlorobenzenesulfonate, m. p. 117-118°. According to literature data, these compounds have the following melting points: 86.5, 110-111 and 118°, respectively [7-9].

TABLE 2

Data on the Quantitative Determination of p-Chlorophenyl p-Chlorobenzenesulfonate in a Ternary Mixture by a Cryoscopic Method

Content in original mixture (in %)			Cont. o-chlorophenyl & 2,4-dichlorophenyl p-chlorobenzenesulfonates after diluting mixt. w. pure p-chlorophenyl p-chlorobenzenesulfonate	Solidification point	Δt	p-Chlorophenyl p-chlorobenzenesulfonate found (in %)
p-chlorophenyl p-chlorobenzenesulfonate	o-chlorophenyl p-chlorobenzenesulfonate	2,4-dichlorophenyl p-chlorobenzenesulfonate				
19.00	8.09	72.91	9.67	80.9°	4.8	18.38
50.00	25.00	25.00	4.55	83.6	2.1	50.16
50.00	40.00	10.00	4.55	83.6	2.1	50.16
60.00	28.00	12.00	10.0	80.7	5.0	59.40

Plotting the fusion diagram of the binary system of p-chlorophenyl p-chlorobenzenesulfonate – o-chlorophenyl p-chlorobenzenesulfonate. We determined the solidification point of the binary system in a normal Beckmann apparatus, used for determining molecular weight by the cryoscopic method. The temperature

was measured with a normal thermometer with 0.1° graduations. Into the apparatus were placed samples of the substances investigated, accurately weighed on analytical balances (with an accuracy of 0.2 mg) and the apparatus was heated on a water bath until the mixture melted completely. The system was then cooled to a temperature 3-3.5° below the expected solidification point of the mixture of substances and the liquid stirred vigorously; crystallization of the substance began immediately and the temperature rose. The highest temperature reached during the crystallization was taken as the solidification point. The determination was carried out not less than 5 times for each mixture and the average values were taken. 10-20 g of substance was used for each determination. The data we obtained are presented in Table 1.

The amount of p-chlorophenyl p-chlorobenzenesulfonate in a mixture was determined under completely analogous conditions.

The cryoscopic constant and the p-chlorophenyl p-chlorobenzenesulfonate content were calculated by the formula used for calculating molecular weight by Raoult's law.

SUMMARY

A study was made of the fusion diagram of the binary system of p-chlorophenyl p-chlorobenzenesulfonate — o-chlorophenyl p-chlorobenzenesulfonate. The cryoscopic constant of p-chlorophenyl p-chlorobenzenesulfonate was determined and a method developed for determining this substance in a mixture with related compounds.

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STUDIES IN ORGANIC INSECTOFUNGICIDES

XL. SYNTHESIS OF SOME NEW SULFAMIDE DERIVATIVES

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In recent years, a large number of substances containing the trichloromethyl mercapto group have been proposed for use as active fungicides in the fight against plant diseases, for treating the seeds of various crops and for the antisepsis of nonmetallic materials. These substances have a low toxicity to plants and a comparatively low toxicity to warm-blooded animals, which is very convenient for their wide use in agriculture. Of this type of compound, above all we should mention the trichloromethylthioamides and imides of various carboxylic and sulfonic acids [1-3], trichloromethyl esters of thiosulfonic acids [4], derivatives of hydantoin, etc.

Under the name of "Captan", the trichloromethylthioamide of tetrahydrophthalic acid has found wide application in various countries of Western Europe and America [5]. This preparation can be used to combat many plant diseases, against which there were no effective preventatives until very recently [6].

In connection with the above, we undertook a special investigation of various groups of organic compounds containing the trichloromethyl mercapto group. First, we synthesized and studied various trichloromethylthioamides of sulfonic acids of the aliphatic and aromatic series. As was found in the work, some amides of sulfonic acids which do not contain trichloromethyl mercapto groups are also active fungicides. In particular, the p-thiocyanoanilides of methane- and p-chlorobenzenesulfonic acids, which are not described in the literature, have a high fungicidal activity.

The amides of sulfonic acids were synthesized by reacting the acid chlorides of appropriate sulfonic acids with excess amines in a hydrophobic organic solvent. The amides of sulfonic acids which we synthesized and which are not described in the literature are presented in Table 1.

TABLE 1

Properties of Sulfamides

| Formula	M. p.	Yield (in %)	% N found	% N calc.
$CH_3SO_2NHC_6H_4SCN-4$	92°	70	12.44, 12.20	12.27
$C_2H_5SO_2NHC_6H_4CH_3-4$	77.5—78	90	7.37, 7.56	7.63
$C_2H_5SO_2NHC_6H_4SCN-4$	101—102	67	12.07, 12.36	11.56
$4-ClC_6H_4SO_2NHC_6H_4SCN-4$	129—130	50	8.60, 8.47	8.61
$4-ClC_6H_4SO_2NHC_6H_4F-4$	110.5—110.8	95	6.35, 6.80	6.63 (F)

The trichloromethylthioamides of sulfonic acids were prepared by reacting perchloromethyl mercaptan with amides of sulfonic acids in an alkaline medium:

TABLE 2

Properties of Trichloromethylthiosulfamides

Formula	M. p.	Yield (in %)	Found (in %)		Calc. (in %)	
			nitrogen	chlorine	nitrogen	chlorine
$CH_3SO_2NC_6H_5$ $\quad\mid$ $SCCl_3$	115—116°	60	—		—	
$CH_3SO_2NC_6H_4Cl$-4 $\quad\mid$ $SCCl_3$	115	65	3.93, 3.92	39.47, 39.35	3.94	39.94
$CH_3SO_2NC_6H_4CH_3$-4 $\quad\mid$ $SCCl_3$	113—113.2	86	3.98, 4.09	31.44, 31.43	4.18	31.78
$CH_3SO_2NC_6H_4SCN$-4 $\quad\mid$ $SCCl_3$	121—121.5	80	7.53, 7.58	27.96, 27.77	7.41	28.19
$C_2H_5SO_2NC_6H_5$ $\quad\mid$ $SCCl_3$	122.7—123	83	4.00, 3.96	31.82	4.18	31.82
$C_2H_5SO_2NC_6H_4Cl$-4 $\quad\mid$ $SCCl_3$	106.8—107.5	60	3.64, 3.70	37.91, 38.50	3.79	38.42
$C_2H_5SO_2NC_6H_4CH_3$-4 $\quad\mid$ $SCCl_3$	105—106	73	3.98, 4.05	30.10, 30.15	4.00	30.50
$C_2H_5SO_2NC_6H_4SCN$-4 $\quad\mid$ $SCCl_3$	118—119	89	7.35, 7.38	27.26, 27.09	7.15	27.15
$4\text{-}ClC_6H_4SO_2NC_6H_5$ $\quad\mid$ $SCCl_3$	116—116.5	78	3.50, 3,65	32.79, 33.20	3.36	34.00
$4\text{-}ClC_6H_4SO_2NC_6H_4Cl$-4 $\quad\mid$ $SCCl_3$	144.5—145	80	3.27, 3.12	38.95, 39.00	3.09	39.17
$4\text{-}ClC_6H_4SO_2NC_6H_4SCN$-4 $\quad\mid$ $SCCl_3$	122—122.5	86	5.73, 5.53	29.81, 29.72	5.90	29.90
$4\text{-}ClC_6H_4SO_2NC_6H_4CH_3$-4 $\quad\mid$ $SCCl_3$	146—146.5	84	3.59, 2.97	32.68, 32.55	3.24	32.89
$4\text{-}ClC_6H_4SO_2NC_6H_4F$-4 $\quad\mid$ $SCCl_3$	126—128	95		4.30 (F)		4.46 (F)

Note: All the trichloromethylthiosulfamides were white crystalline substances, which were practically insoluble in water, but quite readily soluble in organic solvents.

$$RSO_2NHR_1 + CCl_3SCl + NaOH \rightarrow RSO_2N\begin{matrix}R_1 \\ SCCl_3\end{matrix} + NaCl + H_2O.$$
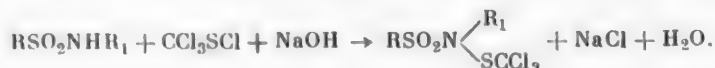
The compounds synthesized and their properties are presented in Table 2 and of them, only three (1, 2 and 10) are described in the literature [7]. It is interesting to note that not all the sulfamides containing the trichloromethyl mercapto group had a high fungicidal activity. Thus, of the compounds synthesized only substances 1-3 and 5-7 (Table 2) were active fungicides. All the other compounds were inactive.

EXPERIMENTAL

The amides of sulfonic acids were prepared, as indicated above, by reacting sulfonyl chlorides with excess amine in a hydrophobic solvent. As an example we will describe the preparation of p-thiocyanophenyl-methanesulfamide. Into a flask with a reflux condenser, a mechanical stirrer and a dropping funnel was placed a solution of 37.5 g of p-thiocyananiline in 100 ml of dry benzene and a solution of 14.3 g of methanesulfonyl chloride in 50 ml of benzene was gradually added with vigorous stirring. When all the methanesulfonyl chloride had been added, the reaction mixture was heated for 2 hours on a water bath. Then after cooling, the

p-thiocyanoaniline hydrochloride was filtered off and washed with benzene and the solvent distilled from the filtrate. The p-thiocyanophenylmethanesulfamide was purified by several recrystallizations. The pure preparation had m. p. 92° (from alcohol).

Found %: N 12.44, 12.20. $C_8H_8N_2S_2$. Calculated %: N 12.27.

All the other amides were prepared under similar conditions. The properties of the amides which are not described in the literature are given in Table 1.

Trichloromethylthioamides of sulfonic acids. Into a flask with a reflux condenser, a mechanical stirrer and a dropping funnel was placed 6.9 g of p-thiocyanophenylmethanesulfamide and 50 ml of 0.5 N sodium hydroxide gradually added, while the mixture was cooled to 10°. With vigorous stirring, 5.6 g of perchloromethyl mercaptan was gradually added to the solution obtained. The perchloromethyl mercaptan was added at 0°. The reaction mixture was then stirred vigorously for 4 hours at 18-22°. During the whole of the reaction, the medium was kept slightly alkaline (to litmus). A thick oily mass first separated and this gradually solidified and changed into a coarse grained precipitate. After the reaction, the precipitate was filtered off, washed with a very small amount of ether (to remove residual perchloromethyl mercaptan) and cold water (to remove sodium chloride), pressed out well on the filter and dried in air. In this way, we obtained a preparation with m. p. 117-120°. The yield of impure product was 10.5 g (80%). The trichloromethylthio-p-thiocyanophenylmethanesulfamide was purified by recrystallization from a mixture of carbon tetrachloride and petroleum ether. The yield of pure material was 6.7 g. The m. p. was 121-121.5°.

Found %: Cl 27.96, 27.77; N 7.53, 7.58. $C_9H_7O_2N_2S_3Cl_3$. Calculated %: Cl 28.19; N 7.41.

The other trichloromethylthioamides of sulfonic acids, presented in Table 2, were prepared under completely analogous conditions.

SUMMARY

In a search for effective fungicides for combating plant diseases, a series of amides and trichlorothioamides, which are not described in the literature, was synthesized. Many of the compounds synthesized were found to be active fungicides.

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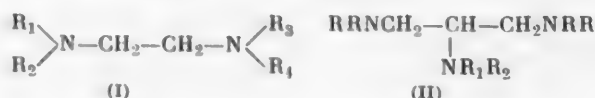
SOME 1,2,3-TRIAMINOPROPANE DERIVATIVES

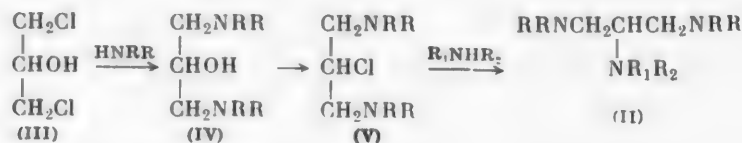## N. K. Kochetkov and L. A. Vorotnikova

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Many aliphatic-aromatic amines are known which have strong and diverse physiological effects. In particular, in this class there is a large group of compounds with a high antihistaminic and spasmolytic acitivity. Of primary importance in this group of compounds are derivatives of N-substituted ethylenediamine of type (I), where R_1 and R_2 are usually aromatic or aliphatic-aromatic and R_3 and R_4 are small aliphatic groups (CH_3, C_2H_5, etc.). A well known representative of this series is, for example, the effective antihistaminic preparation Antergan (I, $R_1 = C_6H_5$, $R_2 = C_6H_5CH_2$, $R_3 = R_4 = CH_3$).

It seemed interesting to determine the physiological activity of compounds of this type containing an extra dialkylaminomethyl group, i.e., previously unknown 1,2,3-triaminopropane derivatives of type (II), whose synthesis is described in the present article. We should note that a communication [1] recently appeared on the high spasmolytic activity of some derivatives of this type.

$$\begin{array}{c} R_1 \\ {}\backslash N-CH_2-CH_2-N{}/ \\ R_2 \end{array} \begin{array}{c} R_3 \\ \\ R_4 \end{array} \qquad \begin{array}{c} RRNCH_2-CH-CH_2NRR \\ | \\ NR_1R_2 \end{array}$$
$$\text{(I)} \qquad\qquad\qquad \text{(II)}$$

We prepared compounds of the 1,2,3-triaminopropane series containing aryl and aralkyl radicals (II; $R_1 = Ar$, $R_2 = ArCH_2$) at the central nitrogen atom, i.e., analogs of Antergan. These compounds were synthesized according to the following scheme.

$$\begin{array}{c} CH_2Cl \\ | \\ CHOH \\ | \\ CH_2Cl \\ \text{(III)} \end{array} \xrightarrow{HNRR} \begin{array}{c} CH_2NRR \\ | \\ CHOH \\ | \\ CH_2NRR \\ \text{(IV)} \end{array} \rightarrow \begin{array}{c} CH_2NRR \\ | \\ CHCl \\ | \\ CH_2NRR \\ \text{(V)} \end{array} \xrightarrow{R_1NHR_2} \begin{array}{c} RRNCH_2CHCH_2NRR \\ | \\ NR_1R_2 \\ \text{(II)} \end{array}$$

Glycerol α, γ-dichlorohydrin (III) was condensed by a known method [1] with a secondary amine, for which we used dimethylamine, diethylamine, piperidine, morpholine and hexamethyleneimine. On treatment with thionyl chloride, the amino alcohols (IV) obtained gave the corresponding amino chlorides (V). The last stage of the synthesis consisted of condensing (V) with secondary amines (of the benzylaniline type), for which we used benzylaniline and p-methoxybenzylaniline. Compound (V) was condensed with the secondary amines by heating the two components in toluene on a water bath in the presence of freshly prepared sodamide. The condensation products (II) obtained in this way were somewhat difficult to isolate since the condensation process was apparently complicated by certain side processes, connected with the possibility of rearrangement of the chloride (V), and also due to the fact that the bases (II) obtained were uncrystallizable, high-boiling oils, which were not quite thermostable. However, distillation of the condensation products in a vacuum of 0.03-0.04 mm yielded substances (II) in a pure form in yields of about 25%; with further and more detailed processing, the yield can undoubtedly be increased. The condensations of 1,3-bis-(N-morpholyl)-2-chloropropane and 1,3-bis-(N-hexamethyleneimino)-2-chloropropane only led to a complex mixture of reaction products. An attempt to prepare crystalline hydrochlorides of the bases (II) was unsuccessful due to their extremely hygroscopic nature.

We were unable to prepare other salts (hydrobromides, sulfates and oxalates) for the same reason. Therefore, aqueous solutions prepared from the base by accurate neutralization with dilute hydrochloric acid were supplied for testing.

TABLE 1

Synthesis of $RRNCH_2CH(OH)CH_2NRR$

Expt. No.	R, R	Solvent	Reaction time and temperature	Yield (in %)	B. p. (pressure in mm)	n^{20}_D
1	CH_3, CH_3	Benzene	2 hr 110—120°* 1 hr 140—150°	86.3	84° (23)	1.4428
2	C_2H_5, C_2H_5	Without solvent	16 hr	70.3	110—112 (10)	1.4538
3	Piperidyl	Acetone	12 hours at room temp. and 1 hour on a water bath	7.3	147—148 (5)	1.4919
4	N-Morpholyl	Acetone		70	149—153 (5)	1.4930
5**	N-Hexamethyleneimino	Acetone		50	159—161 (5)	1.4974

* The reaction was performed in a steel autoclave.
** Found %: N 11.20, 11.27. $C_{15}H_{30}ON_2$. Calculated %: N 11.01.

For characterization, the substances (II) obtained were converted into methiodides, which formed readily when (II) was reacted with methyl iodide in an alcohol medium. It is interesting to note that we obtained only monomethiodides in all cases, despite the use of excess methyl iodide and quite drastic reaction conditions. The methiodides obtained had sharp melting points even before purification, indicating that bases (II) were quite pure substances. The monomethiodides obtained were also of interest from the point of view of their physiological activity.

TABLE 2

Synthesis of $RRNCH_2CHClCH_2NRR$

Expt. No.	R, R	Yield (in %)	B. p. (pressure in mm)	n^{20}_D
1	CH_3, CH_3	80	70° (15)	—
2	C_2H_5, C_2H_5	90	106—108 (8)	—
3	Piperidyl	61	155—157 (11)	1.4949
4 *	N-Morpholyl	40	150—152 (3)	1.4969
5**	N-Hexamethylene-imino	40	155—160 (3)	1.5021

* Found %: N 11.09, 11.15. $C_{11}H_{21}O_2N_2Cl$. Calculated %: N 11.26.
** Found %: N 10.26, 10.35. $C_{15}H_{29}N_2Cl$. Calculated %: N 10.25.

All compounds obtained were tested in the Special Pharmacology Department of the D. A. Kharkevich Institute. The data obtained showed that all the preparations had only very weak and short-term spasmolytic and antihistaminic action. Thus, the introduction of an additional dialkylaminomethyl group into the molecule of an N-substituted ethylenediamine leads to a strong fall in the antihistaminic and spasmolytic activity.

EXPERIMENTAL

1,3-Bis-(dialkylamino)-propanols-2 (IV). 1 mole of glycerol α, γ-dichlorohydrin and 4-5 moles of secondary amine were heated in 150-200 ml of solvent for several hours, cooled, the amine hydrochloride filtered off and the filtrate distilled directly. Data on the reaction conditions and the compounds obtained are presented in Table 1.

1,3-Bis-(dialkylamino)-2-chloropropanes (V). 0.2 mole of thionyl chloride in 20 ml of chloroform was added dropwise to 0.2 mole of amino alcohol (IV) in 80 ml of chloroform and the temperature of the reaction mixture kept at about 0°. The mixture was boiled under reflux for 1 hour, evaporated in vacuum to 1/3 of the total volume at a temperature not exceeding 40°, traces of thionyl chloride removed by the addition and subsequent distillation of benzene, further benzene added, the solution washed with an aqueous solution of potassium carbonate the benzene solution dried over baked potassium carbonate and (V) isolated by vacuum distillation. Data on the compounds obtained are presented in Table 2.

1,3-Bis-(dialkylamino)-2-(N-aryl-N-arylmethyl)-aminopropanes (II). A solution of 0.05 mole of secondary amine (benzylaniline or p-methoxybenzylaniline) in 40 ml of toluene was added to a 0.05 mole suspension of sodamide in 20 ml of dry toluene and heated on a water bath for 2 hours. A solution of 0.05 mole of 1,3-bis-(dialkyl-amino)-2-chloropropane (V) in 30 ml of toluene was added dropwise to the reaction mixture at 30°. The mixture was then heated on a water-bath and stirred for 3 hours, cooled and poured into water. The toluene layer was separated and treated with a dilute solution of hydrochloric acid. The separated acid layer was made alkaline with potassium carbonate and extracted with benzene. The benzene layer was dried with K_2CO_3. (II) was isolated by vacuum distillation. Data on the monomethiodides obtained are presented in Table 3.

TABLE 3

Synthesis of $RRNCH_2CHCH_2NRR$
$\quad\quad\quad\quad\quad |$
$\quad\quad\quad\quad NAr, Ar'$

Expt. No.	R. R	Ar	Ar'	Yield (in %)	B. p. (pressure in mm)	n^{20}_D	% C		% H		M. p. of methiodide
							found	calc.	found	calc.	
1	CH_3, CH_3	C_6H_5	$C_6H_5CH_2$	24.5	143—148° (0.03)	1.5660	77.37, 77.33	77.12	9.45, 9.50	9.39	193—194°
2	C_2H_5, C_2H_5	C_6H_5	$C_6H_5CH_2$	27.4	171—173 (0.03)	1.5469	78.31, 78.32	78.42	10.40, 10.35	10.14	142—144
3	Piperidyl	C_6H_5	$C_6H_5CH_2$	30	215—220 (0.04) *		79.61, 79.67	79.75	9.7, 9.5	9.52	138—140
4	CH_3, CH_3	C_6H_5	$CH_3OC_6H_4CH_2$	21	165 (0.05)	1.5658	73.55, 73.45	73.85	9.23, 9.36	9.15	—

•After long standing the substance crystallized and had m.p. 67.

SUMMARY

1,2,3-Triaminopropane derivatives of the type $Alk_2NCH_2CH(NAr, CH_2Ar)CH_2NAlk_2$ was synthesized by condensation of 1,3-bis-(dialkylamino)-2-chloropropanes with benzylaniline and p-methoxybenzylaniline in the presence of sodamide in toluene.

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INVESTIGATIONS IN THE ISOXAZOLE SERIES

## VIII. ELECTROPHILIC SUBSTITUTION IN ISOXAZOLE

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Despite the considerable amount of work of a preparative character, many of the fundamental problems in the chemistry of isoxazole have remained unstudied up to the present time. Thus, up to the present, the question of the aromatic character of this interesting heterocyclic system and its position among other aromatic heterocycles has not been elucidated completely. In this connection there is great interest in the study of electrophilic substitution reactions in the isoxazole series and comparison of them with the corresponding reactions of benzene and aromatic heterocycles. Although separate examples of nitration [1], sulfonation [2] and halogenation [3] of certain substituted isoxazoles are known, no systematic study of this problem has been carried out and the substitution reactions of isoxazole itself are completely unknown.

We recently studied the nitration, bromination and mercuration of α-phenylisoxazole [4]. The results thus obtained indicated the high activity of the isoxazole nucleus in α-phenylisoxazole, since substitution was directed either mainly or exclusively into the isoxazole nucleus. At the same time, this result does not allow a strict evaluation of the comparative activity of isoxazole and benzene, since attention must be paid to the possible activation of the isoxazole system by the phenyl nucleus and the deactivating effect of the isoxazole nucleus on the benzene ring. To arrive at definite conclusions on the relative activity of compounds of the isoxazole series in electrophilic substitution reactions, we studied the bromination, nitration and sulfonation of the simplest member of this class — isoxazole itself. It was found that in electrophilic substitution reactions isoxazole was much less active then benzene and gave low yields of substitution products.

In the nitration of isoxazole with a mixture of nitric (d 1.50) and sulfuric acids (d 1.84) at room temperature, we isolated a nitro derivative with m. p. 46-47°, whose yield was only 3.5%. This is apparently explained by the fact that the nitration is complicated by simultaneous oxidation processes, since we were unable to isolate unreacted isoxazole. This was also indicated by the intense color of the aqueous solution, formed by treating the reaction mixture with water (evidently, the isoxazole ring was opened). We were unable to find more favorable conditions for the nitration reaction. With nitration under more drastic conditions for example, on raising the temperature to 50-70°, no nitro product at all could be isolated; with the increase in temperature intense decomposition was observed. According to its melting point, the nitro derivative obtained corresponded to 4-nitroisoxazole, which was synthesized earlier from nitromalonaldehyde [5]. Treatment of the nitro derivative we obtained with aniline gave a quantitative yield of the anil of nitrocyanoacetaldehyde. Thus, the nitro group in the nitroisoxazole we obtained could only have occupied position 4.
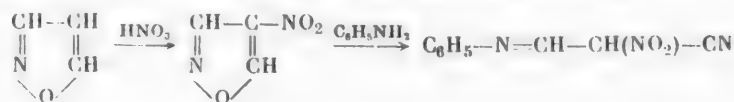

When isoxazole was brominated at room temperature under conditions similar to those for the preparation of bromobenzene, the reaction did not proceed at all. The bromination could only be accomplished by heating isoxazole for 12 hours with an equivalent amount of bromine in the presence of powdered iron. The

yield of a crystalline bromide with m. p. 43-44° was 18%. [*] To prove the structure of the bromo derivative obtained, we cleaved it with sodium ethoxide in alcohol [6]. This treatment yielded the sodio derivative of the enol form of bromocyanoacetaldehyde. This substance, which was obtained as a colorless powder, was very hygroscopic and labile and decomposed completely after 2-3 hours with the liberation of bromine. For this reason, its analysis did not give completely satisfactory results; however, the formation of a bromine-containing derivative when the bromide was treated with sodium alcoholate demonstrated unequivocally that the atom of bromine occupied position 4 in it. Had the bromine occupied any other possible position (3 or 5), then its cleavage with alkali could not have given a compound with the same composition as the sodio derivative we isolated.
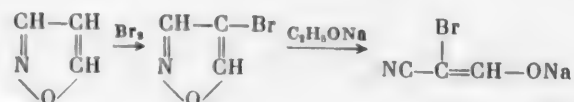
The lability of the substance obtained is quite understandable since the bromine atom in it must be exceptionally labile.

As in the previous case, the sulfonation of isoxazole required more drastic conditions than the sulfonation of benzene. Thus, isoxazole could not be sulfonated by the action of sulfuric acid and 8% oleum, even with prolonged heating. The reaction could be accomplished only by heating isoxazole with 20% oleum for several hours on a boiling water bath. The yield of the sulfonic acid, isolated in the usual way as the barium salt, was 17%. The sulfonic acid was identified as its S-benzylthiuronium salt.
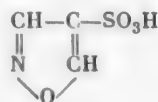
Although we did not prove the position of the sulfonic group in the isoxazole nucleus, there can be little doubt but that the sulfonation, like nitration and bromination, occurred at position 4.

The results we obtained indicate that substitution in the isoxazole nucleus proceeds with much more difficulty than in benzene. Milder electrophilic substitution reactions do not proceed at all with isoxazole. Thus, for example, despite many attempts we were unable to carry out a Friedel – Crafts reaction with isoxazole; the chloromethylation of substituted isoxazoles, which we studied previously[7], gives much lower yields than with the benzene nucleus, while with isoxazole itself, the yield is insignificant.

Substitution in isoxazole is directed overwhelmingly into position 4. We noted this phenomena previously in studying the chloromethylation of isoxazole derivatives [7].

On the basis of the results obtained, we can arrive at the conclusion that isoxazole is similar to pyridine with respect to its capacity for electrophilic substitution reactions, although it differs from the latter in a slightly higher reactivity. This comparison is the more valid as isoxazole is the oxygen isolog of pyridine. Position 4 in the isoxazole nucleus bears a formal analogy to the β-position in the pyridine nucleus and the activity of this position evidently may be explained by the same factors, which determine the activity of the β-position in pyridine.

EXPERIMENTAL

Nitration of isoxazole. At a temperature of −3-0°, 8 g of isoxazole was added to 26 ml of sulfuric acid (d 1.84) with vigorous stirring and strong external cooling [8]. To the mixture obtained was added 26 ml of nitrating mixture (10 ml of nitric acid, d 1.50, and 16 ml of sulfuric acid, d 1.84), while the temperature was

[*]In actual fact the bromination reaction probably proceeded in higher yield , but the bromide obtained was exceptionally volatile and it was impossible to exclude considerable losses during its isolation. Isoxazole could be brominated in chloroform, but the product could not be isolated since it evaporated completely with the solvent.

kept at about 0°. The mixture was stirred for 1 hour at room temperature and for 30 minutes at 35-40°. The reaction mixture was poured onto ice. The solution obtained, which had an intense blue color, was extracted 3 times with ether. The ether extract was dried with calcium chloride. Removal of the ether yielded a yellow oil, which gave off nitrogen oxides strongly and which gave 0.6 g of colorless crystals with m. p. 41-43° when cooled to − 40 to − 50°. The yield was 3.5%. After recrystallization from petroleum ether, the colorless, lustrous plates had m. p. 46-47°. Literature data [5]: m. p. 46°.

Found %: N 24.59, 24.43. C$_3$H$_2$O$_3$N$_2$. Calculated %: N 24.56.

To a solution of 0.1 g of 4-nitroisoxazole in 4 ml of anhydrous alcohol was added 0.1 g of aniline and the mixture obtained was boiled. On cooling, it deposited bright yellow crystals of the anil of nitrocyanoacetaldehyde with m. p. 205-210°. After recrystallization from glacial acetic acid, the lustrous yellow crystals had m. p. 214.5-215.5°(corr.). Literature data [9]: m. p. 215-216° (corr.).

Bromination of isoxazole. 7 ml of bromine was added dropwise with stirring to 10 g of isoxazole containing 0.2 g of iron powder. With the first addition of bromine, a slight evolution of heat was observed. The reaction mixture was heated on a boiling water bath for 12 hours and steam distilled to give an oil, which gave off hydrogen bromide strongly and yielded 4.5 g of colorless crystals with m. p. 43-44° when cooled to −40° to −50°.

Found %: C 24.33, 24.31; H 1.72, 1.57; Br 53.87. C$_4$H$_2$ONBr. Calculated %: C 24.35; H 1.36; Br 54.05.

4-Bromoisoxazole gave colorless, well-formed crystals, which were extremely volatile. After 15 minutes in air, 0.2 g of the substance evaporated completely.

To a solution of 0.5 g of bromoisoxazole in 50 ml of absolute ether was added a solution of 0.08 g of sodium in 5 ml of anhydrous alcohol. When 100 ml of absolute ether had been added to the reaction mixture and the latter shaken for 20 minutes, a colorless precipitate formed and this was filtered off with the exclusion of moisture, washed with absolute ether and dried in vacuum over phosphorus pentoxide.

Found %: C 20.42, 20.18; H 1.78, 1.65. C$_3$HONBrNa. Calculated %: C 21.19; H 0.59.

The sodio derivative of bromocyanoacetaldehyde was an extremely hygroscopic colorless powder, which gave off bromine under the action of moisture.

Sulfonation of isoxazole. A solution of 6.7 g of isoxazole in 10 ml of 20% oleum was heated for 7 hours on a boiling water bath. The sirupy reaction mixture obtained was poured onto ice and neutralized with barium carbonate and the precipitate formed was filtered off. The filtrate was evaporated in vacuum and the colorless crystals which formed were filtered off and dried in vacuum over phosphorus pentoxide. We obtained 3.6 g of barium salt (17% yield), which was recrystallized from water.

Found %: C 16.61, 16.81; H 0.93, 1.01. C$_6$H$_4$O$_8$N$_2$S$_2$Ba. Calculated %: C 16.62; H 0.93.

To a solution of 0.2 g of barium salt of isoxazole-4-sulfonic acid in 3 ml of water was added a solution of 0.2 g of benzylthiuronium chloride in 3 ml of water; colorless, lustrous crystals were deposited and these were filtered off and dried in vacuum over phosphorus pentoxide. We obtained 0.2 g of a substance (76%) with m. p. 136.5-137.5°.

Found %: C 41.68, 41.75; H 4.10, 4.06. C$_{11}$H$_{13}$O$_4$N$_3$S$_2$. Calculated %: C 41.88; H 4.15.

SUMMARY

1. Isoxazole was initrated, brominated and sulfonated and it was shown that electrophilic substitution in the isoxazole nucleus is directed into position 4.

2. It was established that isoxazole is less active than benzene in electrophilic substitution reactions.

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AMINOACYL DERIVATIVES OF NUCLEOSIDES

IV. SYNTHESIS OF N_6-POLYPEPTIDE DERIVATIVES OF 3-β-D-GLUCOPYRANOSYLCYTOSINE BY THE "CARBODIIMIDE" METHOD

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We previously prepared aminoacyl derivatives of cytosine nucleoside by aminoacylation of cytosine nucleoside with mixed anhydrides of cbz*-amino acids and cbz-peptides [1, 2]. However, the yields of aminoacyl nucleosides did not exceed 50% as a rule. It was found that considerably better yields could be obtained by use of the "carbodiimide" method of acylation. This method [3] consists of the aminoacylation of an active amino group of an amino acid or a peptide in the presence of an N,N'-diarylcarbodiimide. The "carbodiimide" method has a series of advantages over the most widely used methods of synthesizing a peptide bond by means of mixed anhydrides of amino acids. The latter are very unstable compounds. They are readily hydrolyzed by water and decompose at a temperature above 0°. The aminoacylation of amino acids and peptides in the presence of a carbodiimide proceeds at room temperature in the presence of moisture and even in an aqueous medium. In addition, the use of the carbodiimide method simplifies the experiment since the free amino acid or peptide is used in the reaction and not their active derivatives. As the condensing agent we used N, N'-dicyclohexylcarbodiimide [4].
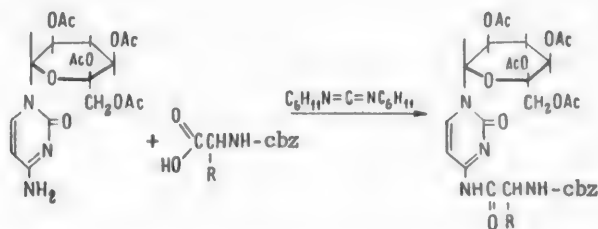
By this method it was possible to increase the yield of N_6-cbz-glycyl-3-β-D-tetraacetylglucopyranosylcytosine to 55% (with the use of mixed anhydrides and yield was 34%) and of N_6-cbz-phenylalanyl-3-β-D-tetraacetylglucopyranosylcytosine to 81% (instead of 55% previously). Similar, polypetide derivatives of cytosine nucleoside may be synthesized from monoacylaminonucleosides.

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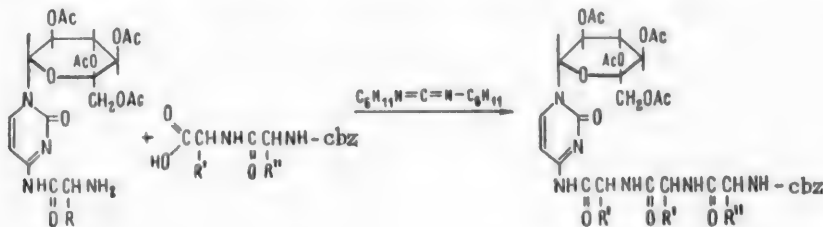
*cbz is carbobenzoxy($C_6H_5CH_2OCO$).

We obtained N_6-cbz-phenylalanyl-S-benzylcysteinyl-, N_6-cbz-valylleucylphenylalanyl- and N_6-cbz-valylphenylalanyl-phenylalanyl-3-β-D-tetraacetylglucopyranosylcytosine in 40-50% yields.

The monoaminoacylnucleosides with a free amino group used in these syntheses were obtained by reduction of the corresponding cbz-derivatives. The reduction was performed with hydrogen over palladium black in an anhydrous dioxane medium at 80-85° for 1.5-2 hours.
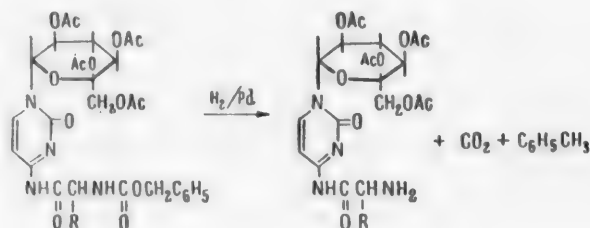
The reaction proceeded similarly if the side chain consisted of three amino acids. In this case we obtained the N_6-tripeptide derivatives of 3-β-o-glucopyranosylcytosine. The compounds synthesized by this method are presented in Table 1.

TABLE 1

N_6-Aminoacyl and N_6-Peptide Derivatives of 3-β-D-Glucopyranosylcytosine
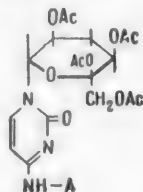
Sub-stance No.	A	Yield (in %)	M. p. (with decomp.)	Absorption maximum in 96% alcohol	
				mµ	ε
(I)	Glycyl	76	86—88°	250	5260
(II)	Leucyl	70	90—94	250	6840
(III)	Phenylalanyl	92	92—94	250	6300
(IV)	Valylglycylphenylalanyl	72	94—97	250	8200
(V)	Valylleucylphenylalanyl	60	98—100	250	7400
(VI)	Valylphenylalanylphenyl-alanyl	68	106—108	250	7860

The polypeptide derivatives of cytosine nucleoside obtained were hydrolyzed with 20% HCl; this caused rupture of the amide and peptide bonds with the formation of a nucleoside and amino acids.
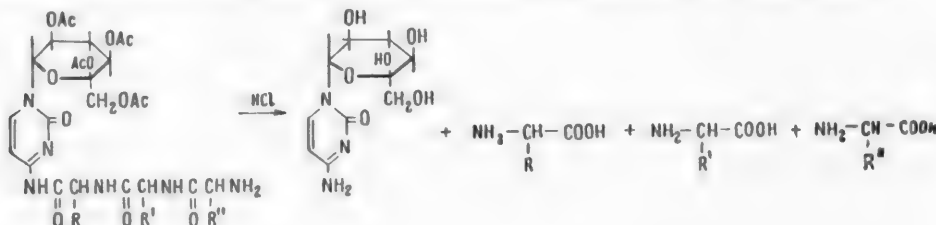
The presence of amino acids in the hydrolyzate was established chromatographically.

It was then interesting to compare the hydrolytic stability of the amide bonds in N_6-cbz-aminoacyl and N_6-cbz-peptide derivatives of 3-β-D-glucopyranosylcytosine [5] with the stability of this bond in the corresponding compounds with the terminal amino group free. Table 2 shows data on the hydrolytic stability of the amide bond in N_6-cbz-phenylalanyl- [5] and N_6-phenylalanyl-3-β-D-tetraacetylglucopyranosylcytosines. The hydrolysis was considered complete when the absorption maximum of the hydrolyzate reached the value 275 mμ, which corresponds to a completely free amino group in cytosine nucleoside [5].

TABLE 2

Hydrolysis of N_6-Phenylalanine Derivative of 3-β-D-Tetraacetyl-glucopyranosylcytosine with a Free and a Protected (with a cbz group) Terminal Amino Group

Character of amino group in aminoacyl residue	Hydrolyzing agent	Hydrolysis temperature	Minimal time required to reach 100% hydrolysis
Free	H_2O	100°	25 hr
Protected	H_2O	100	No hydrolysis after 50 hours
Free	0.01 N NaOH	100	60 min
	0.1 N NaOH	20	15 min
Protected	0.1 N NaOH	100	60 min
Free	0.1 N HCl	20	60 min
Protected	0.1 N HCl	100	15 min

As the results of hydrolysis show, removal of the cbz-group is accompanied by an increase in the lability of the amide bond.

EXPERIMENTAL

I. Synthesis of N_6-cbz-monoaminoacyl and N_6-cbz-dipeptide Derivatives of 3-β-D-Tetraacetylglucopyranosylcytosine

1. N_6-cbz-glycyl-3-β-D-tetraacetylglucopyranosylcytosine. To a solution of 0.025 g of cbz-glycine was added 0.065 g of N,N'-dicyclohexylcarbodiimide, a solution of 0.125 g of 3-β-D-tetraacetylglucopyranosylcytosine hydrochloride [2] in 5 ml of dioxane and 0.25 ml of 1 N NaOH. The reaction mixture was left at room temperature for 4 hours. After 10-15 minutes, the reaction mixture began to become turbid and toward the end of the reaction, a voluminous precipitate of dicyclohexylurea formed. The precipitate was filtered off and the solution evaporated in vacuum. The residual oil was dissolved in 5 ml of chloroform. The solution was washed with acetic acid, water, 2 N sodium carbonate solution and again with water. The solution was dried over Na_2SO_4 and 15-20 ml of absolute petroleum ether added. The precipitate was filtered off and washed with absolute petroleum ether. The yield was 0.085 g (54%) and the decomposition point 119-121°; the melting point of a preparation obtained previously [2] was not depressed.

The following substances were prepared in the same way.

2. N_6-cbz-leucyl-3-β-D-tetraacetylglucopyranosylcytosine. The yield was 17%. The decomposition point was 140°.

Found %: N 8.50. $C_{32}H_{40}O_{13}N_4$. Calculated %: N 8.14.

3. N_6-cbz-phenylalanyl- 3-β-D-tetraacetylglucopyranosylcytosine. The yield was 81%. The decomposition point was 143-145°. No depression in melting point was observed with a preparation obtained previously [1].

4. N_6-cbz-phenylalanyl-S-benzylcysteinyl-3-β-D-tetraacetylglucopyranosylcytosine. The yield was 38%. The decomposition point was 80-81°. The UV absorption in 96% alcohol: λ_{max} 250, 300 mμ (ϵ 8630, 4200).

Found %: N 7.86. $C_{45}H_{49}O_{14}N_5S$. Calculated %: N 7.65.

II. Synthesis of N_6-cbz-tripeptide Derivatives of 3-β-D-Tetraacetylglucopyranosylcytosine

1. N_6-cbz-valylglycylphenylalanyl-3-β-D-tetraacetylglucopyranosylcytosine. The substance was prepared by the procedure described above (I, Expt. 1) from N_6-phenylalanyl-3-β-D-tetraacetylglucopyranosylcytosine (III, Expt. 1) and cbz-valylglycine in the presence of N,N'-dicyclohexylcarbodiimide. The yield was 38% and the decomposition point 104-106°. The substance was readily soluble in the usual organic solvents, but sparingly so in petroleum ether and water. The substance was dried in vacuum over P_2O_5 for 60 hours before analysis.

Found %: C 55.61; H 5.91; N 9.2. $C_{42}H_{50}O_{15}N_6$. Calculated %: C 55.17; H 5.91; N 9.19.

UV absorption in 96% ethyl alcohol: λ_{max} 250 mμ (ϵ 4800).

50 mg of the substance was heated at 100° with 5 ml of 20% HCl for 15 hours. The hydrolyzate was chromatographed on paper in an n-butanol − acetic acid − water (4:1:5) medium. The chromatogram was developed with ninhydrin. We found valine, glycine and phenyl alanine, whose R_f values agreed with those of the amino acids put onto the chromatogram in parallel as "references".

The following substances were prepared in the same way.

2. N_6-cbz-valylphenylalanylphenylalanyl-3-β-D-tetraacetylglucopyranosylcytosine. The yield was 46%. The decomposition point was 103-105°. The substance was dried in vacuum over P_2O_5 for 60 hours before analysis.

Found %: N 8.73. $C_{49}H_{56}O_{15}N_6$. Calculated %: N 8.67.

UV absorption in 96% ethyl alcohol: λ_{max} 250 mμ (ϵ 7800).

50 mg of the substance was heated at 100° with 5 ml of 20% HCl for 15 hours. The hydrolyzate was chromatographed on paper in an n-butanol − acetic acid − water (4:1:5) medium. * The chromatogram was developed with ninhydrin. We found valine and phenylalanine, whose R_f values agreed with those of amino acids put onto the paper in parallel as "references".

3. N_6-cbz-valylleucylphenylalanyl-3-β-D-tetraacetylglucopyranosylcytosine. The yield was 32%. The decomposition point was 108-110°. The substance was dried in vacuum over P_2O_5 for 60 hours before analysis.

Found %: N 9.22. $C_{46}H_{52}O_{15}N_6$. Calculated %: N 8.99

UV absorption in 96% ethyl alcohol: λ_{max} 250 mμ (ϵ 6400).

III. Removal of the cbz-group by Reduction with Hydrogen over Pd-Black

1. Preparation of N_6-phenylalanyl-3-β-D-tetraacetylglucopyranosylcytosine. A stream of dry hydrogen was passed into a solution of 0.2 g of N_6-cbz-phenylalanyl-3-β-D-tetraacetylglucopyranosylcytosine in 25 ml of absolute dioxane, conatining 10 mg of Pd-black and heated to 80-90°. The course of the reduction was followed by the turbidity of barium hydroxide solution. The reduction was complete after 1.5-2 hours. The solution was centrifuged and evaporated to dryness in vacuum. The crystalline substance was transferred to a glass filter and washed with cold benzene and then with ether. The yield was 0.143 g. The substance was readily soluble in alcohol, chloroform and dioxane and sparingly soluble in ether, benzene and water. It was dried in vacuum over P_2O_5 for 20 hours at 65° before analysis.

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*Paper from the Leningrad factory.

When boiled with water for 10-15 minutes, it gave a clear ninhydrin reaction. Data on the hydrolysis of N_6-phenyalanyl-3-β-D-tetraacetylglucopyranosylcytosine are presented in Table 2. We described the hydrolysis procedure previously [5]. The phenylalanine formed during acid and alkaline hydrolysis was identified by paper chromatography.

The other substances listed in Table 1 were prepared similarly. The analyses are presented in Table 3.

TABLE 3

Sub-stance-No.	Empirical formula	N content (in %)	
		found	calc.
(I)	$C_{20}H_{26}O_{11}N_4$	*	—
(III)	$C_{27}H_{32}O_{11}N_4 \cdot H_2O$	**	—
(IV)	$C_{3:}H_{44}O_{13}N_6$	11.02	11.30
(V)	$C_{38}H_{46}O_{13}N_6$	10.41	10.59
(VI)	$C_{41}H_{50}O_{10}N_6$	10.31	10.47

*Found %: C 48.00; H 5.07. Calculated %: C 48.19; H 5.22.
**Found %: C 53.61; H 5.78. Calculated %: C 53.46; H 5.61.

2. N_6-Glycyl-3-β-D-tetraacetylglucopyranosylcytosine. The substance was soluble in alcohol, dioxane and chloroform and difficultly soluble in ether, benzene and water. Before analysis, it was dried over P_2O_5 in vacuum at 65° for 60 hours.

The substance did not give a ninhydrin reaction, even on prolonged boiling with water. By the Van Slyke method, 16% of amine nitrogen was found after 5 minutes and 82% after 25 minutes.

SUMMARY

1. Aminoacyl derivatives of cytosine nucleoside may be prepared in good yields by the acylation of a nucleoside with cbz-amino acids and cbz-peptides in the presence of N,N'-dicyclohexylcarbodiimide.

2. N_6-Aminoacyl and N_6-peptide derivatives of 3-β-D-glucopyranosylcytosine with a free amino group in the aminoacyl chain were prepared.

3. It was established that the amide bond in N_6-aminoacyl derivatives of 3-β-D-glucopyranosylcytosine with a free amino group in the aminoacyl chain are hydrolyzed considerably more easily than in the corresponding cbz-derivatives.

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REACTION OF ETHERS WITH ANILINE AND AMMONIA

III. ALKYLATION OF ANILINE WITH DIMETHYL ETHER

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The catalystic alkylation of aniline with ethers in the vapor-gas phase is of considerable practical inter-est [1]. Dimethylaniline is prepared from aniline and dimethyl ether in the presence of active aluminum oxide on an industrial scale [2]. In work on the alkylation of aromatic amines with ethers, consideration has largely been given to applied problems such as choice of catalysts, choice of optimal conditions, etc. [3-8]. There have been no investigations devoted to studying the kinetics and mechanism of these reactions. In this connec-tion, we studied the kinetics of the alkylation of aniline by dimethyl ether. This reaction proceeds extremely smoothly in the presence of active aluminum oxide in the range 235-300° without any side reactions [7-9].

Preliminary thermodynamic calculation of the reactions

$$C_6H_5NH_2 + (CH_3)_2O \rightleftharpoons C_6H_5NHCH_3 + CH_3OH \tag{I}$$
$$C_6H_5NHCH_3 + (CH_3)_2O \rightleftharpoons C_6H_5N(CH_3)_2 + CH_3OH \tag{II}$$

showed that processes tending toward the formation of aliphatic-aromatic amines were favored (Table 1).

TABLE 1

Process temp. reaction No.	200°		250°		300°	
	K_e	yield (in %)	K_e	yield (in %)	K_e	yield (in %)
(I)	64.90	89.10	45.70	87.10	32.60	85.10
(II)	117	91.4	71.2	89.5	48.4	87.4

The thermodynamic calculations were carried out by the procedure described previously [18], using the most reliable thermodynamic constants [10-13]. Table 1 gives the equilibrium constants K_e and the yields; the latter were calculated for an equimolecular mixture.

Experimental Procedure

The reaction kinetics of the alkylation of aniline with dimethyl ether were studied in a circulating flow apparatus (Fig. 1). The dimethyl ether was obtained by dehydration of methanol over active aluminum oxide at 260-280° in a catalytic furnace (1), freed from water and alcohol vapor by passage through a system of traps, filled successively with water (2), calcium chloride (3) and solid potassium hydroxide (4) and fed through a flow meter (5) into the aniline evaporator (6); simultaneously, liquid aniline was fed into the evaporator through a calibrated capillary from a burette (7) and evaporated in a stream of dimethyl ether vapor at 240°. The mixture
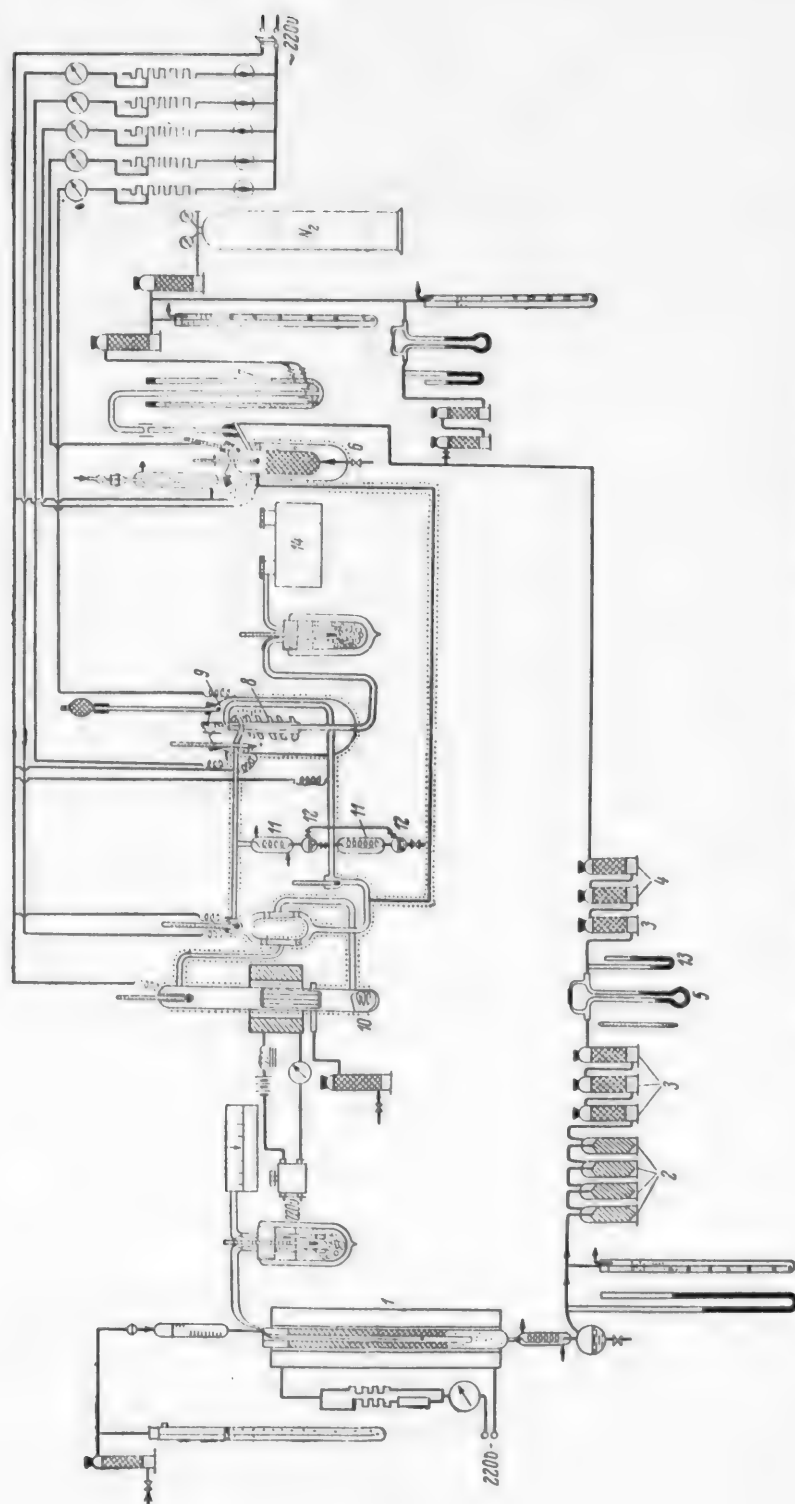
Fig. 1. Plan of circulating flow apparatus. Explanation in text.

of dimethyl ether and aniline vapor obtained was led from the evaporator into the circulating system, which consisted of the catalyst tube (8) and a spiral for heating the circulating gas-vapor mixture to the desired temperature, a glass bath (9), a glass electromagnetic circulating pump (10) and two receivers (11) for the catalyzate before and after the catalyst tube. The whole circulating apparatus was joined together in one piece and made from molybdenum glass. To prevent condensation of the vapor-gas mixture, the apparatus was fitted with a sectional electric heater, which made it possible to maintain the desired temperature at all points of the apparatus. The circulation rate was 480 liters/hour. The steady continuous take off of samples was controlled by cocks (12). The pressure in the circulating apparatus was measured with a manometer (13). To maintain the desired temperature in the catalyst tube, the bath was loaded with a heat-transfer agent with an appropriate boiling point; temperature variations in the catalyst zone during an experiment did not exceed $\pm$ 0.2°. The temperature was measured with a thermocouple connected to a potentiometer (14).

Samples of catalyzate were withdrawn before and after the catalyst tube, dried over fused sodium hydroxide, distilled from a Wurtz flask and analyzed separately for primary, secondary and tertiary amine contents by Nelyubina's method [14]. The catalyzate obtained in the alkylation of methylaniline with dimethyl ether was analyzed refractometrically [15].

The dimethyl ether used in the experiments had b. p. 23.7° at 760 mm. The "pure" grade aniline was distilled and had the following constants: solidification point −6.3, d^{20}_4 1.022, $n^{20}D$ 1.5852.

The catalyst used was active aluminum oxide with a bulk weight of 0.4 g/cc and a specific surface of 270 m^2/g.

Experimental Results and Discussion

To determine the effect of diffusion on the reaction kinetics of aniline alkylation with dimethyl ether over the temperature range 210-280° investigated, tests were carried out with active aluminum oxide with grain sizes of 4-5, 0.25-1.0 and 0.10-0.25 mm (Table 2).

TABLE 2

Grain size of catalyst (in mm)	Composition of catalyzate (in weight %)		
	aniline	methylaniline	dimethylaniline
4—5	33.03	19.40	47.57
0.25—1.0	28.46	23.07	48.47
0.10—0.25	28.87	23.60	47.53

Note. Amount of catalyst, 1.0006-1.0018 g, duration of experiment, 1.5 hours, aniline consumption, 4.93-5.10 ml/hour; consumption of dimethyl ether, 115.5 ml/min and temperature of process, 279°.

As the data in Table 2 show, diffusion retardation of the process on active aluminum oxide with a grain size of 0.10-0.25 and 0.25-1.00 is practically absent. In all subsequent experiments we used a catalyst with a grain size of 0.25-1.00 mm, prepared from one batch of active aluminum oxide. Each experiment was performed with a fresh portion of catalyst, whose activity remained constant during the course of the experiment.

The results of experiments carried out to study the dependence of catalyzate composition on the temperature and the amount of active aluminum oxide loaded into the catalytic apparatus are shown in Fig. 2. In these experiments, a constant amount of aniline of 5.62 ± 0.05 g/hour and of dimethyl ether of 115.5 ml/min was fed into the circulating flow apparatus. The form of the curves has the same character for all temperatures: the amount of aniline falls continuously and the methylaniline content of the catalyzate first grows rapidly, then slows down and, as can be seen from the experiments at 256 and 281° (Fig. 2), passes through a maximum. The curve illustrating the change in the amount of dimethylaniline in the catalyzate shows a continuous increase in the dimethylaniline and has an inflection. The form of the curves obtained in the alkylation of aniline

with dimethyl ether are characteristic of successive reactions and show that the alkylation of aniline consists of successive substitution of the hydrogen atoms on the nitrogen by the alkyl radicals of the ether and may be represented by reactions (I) and (II). This conclusion is confirmed by the presence of considerable amounts of alcohol in, and the absence of alcohol from the catalyzate in the initial stage of the alkylation. The reaction
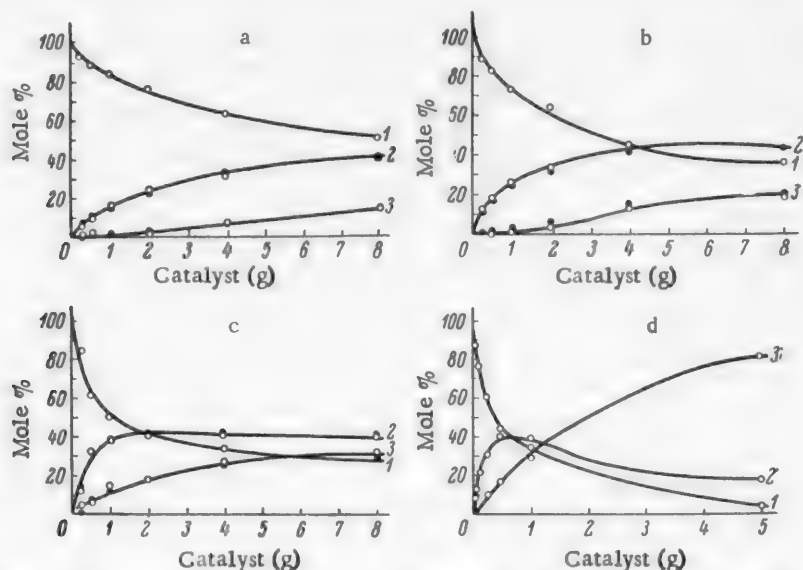

Fig. 2. Kinetics of the alkylation of aniline by dimethyl ether on active aluminum oxide at 212.7° (a), 230° (b), 256° (c) and 281° (d): 1) aniline, 2) methylaniline and 3) dimethylaniline.

scheme, (I) and (II), was confirmed by a series of experiments on the alkylation of the intermediate product, monomethylaniline, with dimethyl ether (1 : 4.77) at 211.4, 231 and 251° (Fig. 3). At high aniline conversions, as methanol is formed, the dehydration of methanol by equation (III) may proceed.

$$2CH_3OH \rightleftarrows CH_3OCH_3 + H_2O \qquad\qquad (III)$$

If we start from Langmuir's theory of heterogeneous processes, then the alkylation of aniline by the ether in a circulating flow system may be represented by the following equations:

$$\frac{U \cdot x}{G} = k_1' \sigma_A \sigma_{ME} =$$

$$= k_1' \frac{b_A b_{ME} P^2 (a-x)(b-x-y+z/2)}{\{a+b+[b_A(a-x)+b_{MA}(x-y)+b_{DA}y+b_{ME}(b-x-y+z/2)+b_{AL}(x+y-z)+b_W \cdot z/2]P\}^2} \qquad (1)$$

$$\frac{U \cdot y}{G} = k_2' \sigma_{MA} \sigma_{ME} =$$

$$= k_2' \frac{b_{MA} \cdot b_{ME} P^2 (x-y)(b-x-y+z/2)}{\{a+b+[b_A(a-x)+b_{MA}(x-y)+b_{DA}y+b_{ME}(b-x-y+z/2)+b_{AL}(x+y-z)+b_W \cdot z/2]P\}^2} \qquad (2)$$

where: U — volume of the gaseous mixture withdrawn from the circulating flow apparatus (liter/hour); G — weight of catalyst (g); a — initial concentration of aniline (mole/liter); b — initial concentration of dimethyl ether (mole/liter); x — decrease in aniline (mole/liter); y — concentration of dimethylaniline (mole/liter); z — decrease in methanol (mole/liter); P — total pressure of vapor gas mixture (atm.); σ_A — fraction of unit area of the catalyst occupied by aniline; σ_{MA} — fraction of unit area of catalyst occupied by methylaniline; σ_{ME} — fraction of unit area of catalyst occupied by dimethyl ether; k_1' and k_2' — reaction rate constants

of the first and second stage of aniline alkylation by dimethyl ether: b_A, b_{ME}, b_{MA}, b_{DA}, b_{AL} and b_W — the corresponding absorption coefficients.
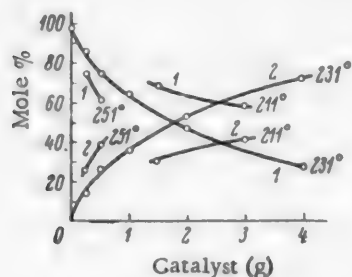

Fig. 3. Kinetics of the alkylation of methylaniline with dimethyl ether on active aluminum oxide at 211.4, 231 and 251°: 1) methylaniline and 2) dimethylaniline.

In this case the rate of the reverse processes is neglected as with a large excess of dimethyl ether the given reactions proceed practically to completion.

By dividing (2) by (1) we obtain ratio (3).

$$\frac{y}{x} = K\ \frac{x-y}{a-x}, \text{where} \quad K = \frac{k_2' \cdot b_{MA}}{k_1' b_A} \quad (3)$$

This ratio makes it possible to calculate the possible composition of products formed during the reaction. Figure 4 shows a comparison of the experimental data (points plotted) with the theoretical curves of the dependence of the methylaniline (x-y) and dimethylaniline (y) content as a function of the degree of conversion of the aniline (x), calculated from equation (3).
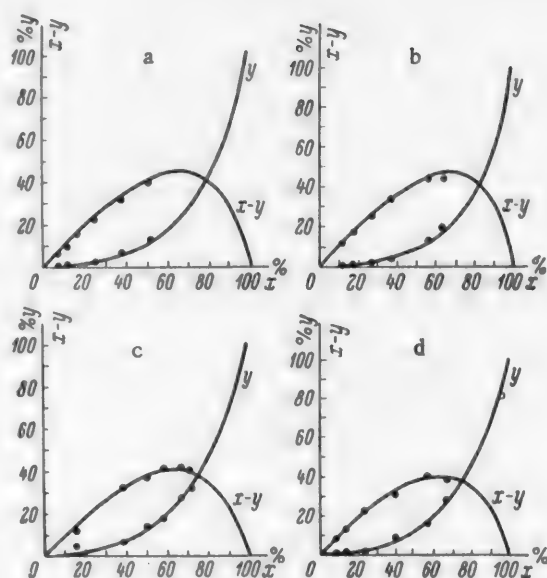
Fig. 4. Dependence of catalyzate composition on degree of conversion of aniline at 212.7° (a), 230° (b), 256° (c) and 281° (d). x— amount of reacted aniline, x-y — concentration of methyaniline in catalyzate and y — concentration of dimethylaniline in catalyzate.

TABLE 3

Reaction temperature	k_1	$K = \frac{k_2}{k_1}$	k_2	E_1 (cal / mole)	E_2(cal / mole)
212.7°	3.70	0.25	0.94		
230.0	8.95	0.21	1.85	23000	24000
256.0	31.2	0.33	10.32		
281.0	71.9	0.33	23.38		

The graphs presented show that catalyzate compositions obtained experimentally agree well with the values calculated theoretically for successive reactions, occurring in a circulating flow apparatus.

The rate of aniline alkylation by dimethyl ether over active aluminum oxide is described satisfactorily by empirical equation (4) within the limits of 212.7-256°.

$$k_1 = \frac{U \cdot x}{G} \cdot \frac{\sqrt{x-y}}{(a-x)(b-x-y)} \quad (4)$$

As the equation given shows, the alkylation of aniline by dimethyl ether is retarded by the reaction products.

On the basis of the experimental data, the reaction rate constants for the first and second stages and also their ratio were calculated from equations (3) and (4) (Table 3).

The data presented in Table 3 show that the rate constant of reaction (I) is approximately 3 times greater than the rate constant of reaction (II). With an increase in temperature there is some tendency for the ratio of the reaction rate constants to increase, indicating a more rapid growth in the rate of methylaniline alkylation in comparison with the rate of aniline alkylation. The activation energies of the two stages of the reaction were calculated from the rate constants (Table 3).
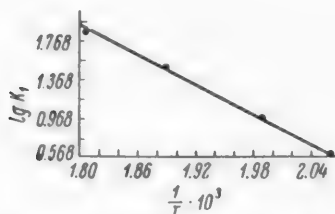

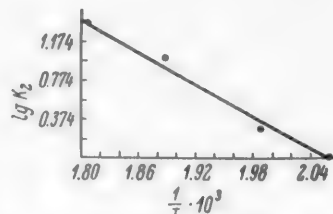Fig. 5. Dependence of log K_1 on the inverse temperature.

Fig. 6. Dependence of log K_2 on the inverse temperature.

From the experimental data we can conclude that the alkylation of aniline by dimethyl ether on active aluminum oxide proceeds through successive stages of substitution of hydrogen atoms at the nitrogen by the methyl radicals of the ether with the simultaneous formation of methanol by schemes (I) and (II). The reaction scheme given may be considered general for the reactions of other ethers with ammonia and different amines in the presence of dehydrating oxide catalysts [18, 19].

In conclusion we should note that the very widely held opinion that in the reaction of ethers with amines or ammonia there occurs the simultaneous substitution of both hydrogen atoms at the nitrogen by the corresponding radicals of the ether with the simultaneous formation of water [5, 8, 16, 17] must be considered incorrect.

SUMMARY

1. A study was made of the alkylation of aniline by dimethyl ether in a circulating flow apparatus.

2. It was shown that the methylation of aniline on active aluminum oxide proceeds with the successive substitution of the hydrogen atoms at the nitrogen by alkyl groups.

3. The activation energies and the ratio of the rate constants of the two stages of the process were calculated.

4. An empirical equation is given for calculating the rate constants of the reaction.

5. A scheme is proposed for the reaction of ethers with amines and ammonia.

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# FLUORINE-CONTAINING ARYL TRICHLOROPHOSPHAZOSULFONES AND THEIR DERIVATIVES

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At the present time a series of insecticides is known in which the molecules contain an atom of fluorine [1]. In this respect there is particular interest in preparations containing atoms of both fluorine and phosphorus [2]. The purpose of the present work was the synthesis and a study of the insecticide properties of aryl trichlorophosphazosulfones and their derivatives with atoms of fluorine or trifluoromethyl groups as substitutents in the aromatic nucleus. For this purpose we prepared p-fluorobenzenesulfonamide [3] and the previously unknown m-trifluoromethylphenylsulfonamide. The latter was prepared by the scheme:
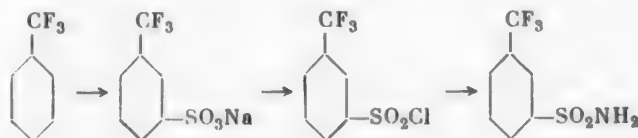
Its structure was proved by its conversion into m-carboxybenzenesulfonamide [4], when it was heated with sulfuric acid. Reaction of the sulfonamides obtained with phosphorus pentachloride gave aryl trichlorophosphazosulfones [5].

$$Ar{-}SO_2NH_2 + PCl_5 \rightarrow Ar{-}SO_2N{=}PCl_3$$
$$Ar = p{-}FC_6H_4 \ (I), \ m{-}CF_3C_6H_4 \ (II).$$
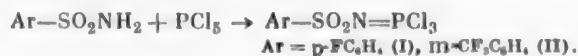
Hydrolysis or acidolysis of the trichlorophosphazo compounds (I) and (II) yielded diacid chlorides and the corresponding phenylsulfonamidophosphoric acids.

The monoacid chloride of p-fluorophenylsulfonamidophosphoric acid was also isolated.

$$p{-}FC_6H_4SO_2N{=}PCl_3 \rightarrow p{-}FC_6H_4SO_2NHPOCl_2 \rightarrow$$

$$\rightarrow p{-}FC_6H_4SO_2NHP{\overset{O}{\underset{Cl}{\diagup}}}OH \rightarrow p{-}FC_6H_4SO_2NHP{\overset{O}{\underset{OH}{\diagup}}}OH$$
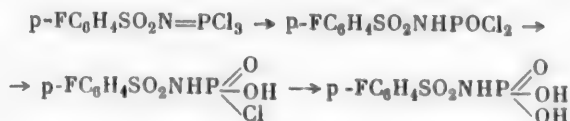
When condensed with alcoholates and phenolates, compounds (I) and (II) gave esters. The data on them are presented in Tables 1 and 2.

The esters of p-fluoro- and m-trifluoromethylsulfonamidophosphoric acids were colorless crystalline substances (with the exception of the liquid triethyl esters), which were insoluble in water, readily soluble in alcohol, acetone and benzene and difficultly soluble in petroleum ether. Preparations 1 and 7 (Table 1) had a certain insecticide activity.

TABLE 1

p-Fluoro- and m-Trifluoromethylphenyl Trialkoxyphosphazosulfones and Triaroxyphosphazosulfones $RC_6H_4SO_2N = P(OR')_3$

Preparation No.	R	R'	Yield (in %)	M. p.	Recrystallization solvent	Empirical formula	% N found	% N calc.	Yield of $RC_6H_4SO_2NHPO(OR')_2$ (in %)
1	p-F	CH_3	36.3	45—46°	Benzene with petroleum ether	$C_9H_{12}O_5NSPF$	4.95, 4.97	4.72	26.4
2	p-F	C_2H_5	65.2	*	—	$C_{12}H_{19}O_5NSPF$	4.25, 4.30	4.13	5.2
3	p-F	C_6H_5	23.8	69—70	Aqueous alcohol	$C_{24}H_{19}O_5NSPF$	3.13, 3.22	2.90	12.7
4	p-F	$p\text{-}FC_6H_4$	37.2	70—72	The same	$C_{24}H_{16}O_5NSPF_4$	2.85, 2.94	2.62	14.2
5	p-F	$p\text{-}ClC_6H_4$	53.5	115—116	*	$C_{24}H_{16}O_5NSPCl_3F$	***		6.2
6	p-F	$p\text{-}NO_2C_6H_4$	80.0	180—181	Benzene	$C_{24}H_{16}O_{11}N_4SPF$	9.14, 9.20	9.05	Not isolated
7	m-CF₃	CH_3	59.0	58—60	CCl₄ with petroleum ether	$C_{10}H_{12}O_5NSPF_3$	4.34, 4.47	4.14	22.5
8	m-CF₃	C_2H_5	85.8	**	—	$C_{13}H_{19}O_5NSPF_3$	3.66, 3.94	3.60	4.3
9	m-CF₃	$p\text{-}NO_2C_6H_4$	84.2	167—168	Benzene	$C_{27}H_{16}O_9N_4SPF_3$	8.40, 8.43	8.40	Not isolated

*B. p. 202-204° (10 mm).

**B. p. 185-187° (7 mm).

***Found %: Cl 17.96, 18.01. Calculated %: Cl 18.30.

TABLE 2

Diesters of p-Fluoro- and m-Trifluoromethylphenylsulfonamidophosphoric Acids $RC_6H_4SO_2NHPO(OR')_2$

R	R'	Yield (in %)	M. p.	Recrystallization solvent	Empirical formula	% N found	% N calc.
p-F	CH_3	66.5	145—146°	Benzene	$C_8H_{11}O_5NSPF$	4.99, 5.17	4.95
p-F	C_2H_5	80.8	118—119	Aqueous alcohol	$C_{10}H_{15}O_5NSPF$	4.59, 4.64	4.50
p-F	C_6H_5	12.7 *	183—184	The same	$C_{18}H_{15}O_5NSPF$	3.67, 3.71	3.44
p-F	$p\text{-}FC_6H_4$	14.2 *	142—143	*	$C_{18}H_{13}O_5NSPF_2$	3.36, 3.50	3.17
p-F	$p\text{-}ClC_6H_4$	6.2 *	149—150	*	$C_{18}H_{13}O_5NSPCl_2F$	**	
p-F	$p\text{-}NO_2C_6H_4$	88.6	177—178	*	$C_{18}H_{13}O_9N_3SPF$	8.59, 8.66	8.45
m-CF₃	CH_3	22.5 *	93—94	Benzene with petroleum ether	$C_9H_{11}O_5NSPF_3$	4.38, 4.48	4.21
m-CF₃	$p\text{-}C_2H_5$	91.3	71—73	Aq. alcohol	$C_{11}H_{15}O_5NSPF_3$	4.12, 4.18	3.87
m-CF₃	$p\text{-}NO_2C_6H_4$	88.0	194—195	The same	$C_{19}H_{13}O_9N_3SPF_3$	7.79, 7.90	8.16

*Isolated in the preparation of compounds of the type $RC_6H_4SO_2N = P(OR')_3$

**Found %: Cl 15.21, 15.17. Calculated %: Cl 14.90.

EXPERIMENTAL

p-Fluorobenzenesulfonamide was prepared by the reaction of fluorobenzene with chlorosulfonic acid and subsequent treatment of the p-fluorobenzenesulfonyl chloride obtained with a 25% aqueous ammonia solution. The yield was 60%, calculated on fluorobenzene. The m. p. was 125-126° (126° [3]).

p-Fluorophenyl trichlorophosphazosulfone. 0.1 mole of p-fluorobenzenesulfonamide was mixed with 0.103 mole of PCl_5 and heated at 105-108° until the evolution of HCl ceased (1.5 hours). The reaction mixture was heated in vacuum to remove the excess PCl_5. When cooled to room temperature, the product crystallized. The yield was 99.0%. After recrystallization from petroleum ether, the material had m. p. 72-73°.

Found: equiv. after hydrolysis, 4.93 and 5.02. $C_6H_4O_2NSPCl_3F$. Calculated: equiv. after hydrolysis, 5.00.

Diacid chloride of p-fluorophenylsulfonamidophosphoric acid. A mixture of 0.01 mole of (I), 0.01 mole of formic acid and 20 ml of benzene was heated to 85° and left overnight. The precipitate was filtered off and washed with benzene. The yield was 96.4%. The m. p. was 135-136. (from benzene).

Found: equiv. after hydrolysis, 3.98, 4.00. $C_6H_5O_3NSPCl_2F$. Calculated: equiv. after hydrolysis, 4.00.

Monoacid chloride of p-fluorophenylsulfonamidophosphoric acid. A mixture 0.01 mole of the diacid chloride of p-fluorophenylsulfonamidophosphoric acid, 0.01 mole of anhydrous formic acid and 20 ml of benzene was heated for 1.5 hours at 80-85°. The following day, the product crystallized. The yield was 86.5%. The m. p. was 123-124° (from benzene).

Found: equiv. after hydrolysis, 2.90, 2.93. $C_6H_6O_4NSPClF$. Calculated: equiv. after hydrolysis, 3.00.

p-Fluorophenylsulfonamidophosphoric acid. A mixture of 0.01 mole of the diacid chloride of p-fluorophenylsulfonamidophosphoric acid, 0.01 mole of anhydrous formic acid and 10 ml of benzene was heated for 1.5 hours at 80-85°. Then a further 0.01 mole of anhydrous formic acid was added and the mixture heated for a further 4 hours. At the end of the reaction, the evolution of HCl ceased and a crystalline precipitate formed. After cooling, the product was filtered off and washed with benzene and ether. The yield was 39.0%. The m. p. 148-149°.

Found: equiv. after hydrolysis, 1.94, 1.96. $C_6H_7O_4NSPF$. Calculated: equiv. after hydrolysis, 200.

m-Trifluoromethylbenzenesulfonamide. 29.2 g of benzotrifluoride was added at −2° to 25 g of 62% oleum. The mixture was stirred for 2 hours at 0° and left for 1 day at room temperature. The reaction mixture was then poured onto 300 ml of saturated NaCl solution cooled to 0° and the precipitate filtered off and washed with NaCl solution. It was dried at 120°. The yield of the technical product was 43.5 g (88.2%). 43.5 g of the sodium salt of m-trifluoromethylbenzenesulfonic acid was mixed with 42.5 g of PCl_5, heated for 3 hours at 130-140°, cooled, poured into 400 ml of water with ice, shaken and the product extracted with ether. The ether solution was dried. The ether was removed and the product vacuum distilled. The yield of m-trifluoromethylbenzenesulfonyl chloride was 28.2 g (65.0%). The b. p. was 88-90° at 6 mm. Into an ice-water cooled solution of 34.4 g of the acid chloride of m-trifluorobenzenesulfonic acid in 60 ml of benzene was passed ammonia. The benzene was distilled off. The amide was washed with water and recrystallized from aqueous methyl alcohol. The yield was 19.8 g (88.0%). The m. p. was 121-122°.

Found %: N 6.23, 6.25. $C_7H_6O_2NSF_3$. Calculated %: N 6.22.

M-Trifluoromethylphenyl trichlorophosphazosulfone was prepared similarly to the p-fluoro derivative. The yield was 99.0%. The m. p. was 52-54° (from petroleum ether).

Found: equiv. after hydrolysis, 4.92, 4.97. $C_7H_4O_2NSPCL_3F_3$. Calculated: equiv. after hydrolysis, 5.0.

The diacid chloride of m-trifluoromethylbenzenesulfonamidophosphoric acid was prepared as above. The yield was 84.5%. The m. p. was 82-83° (from a mixture of benzene and petroleum ether).

Found: equiv. after hydrolysis, 3.93, 3.94. $C_7H_5O_3NSPCL_2F_3$. Calculated: equiv. after hydrolysis, 4.0.

m-Trifluoromethylphenylsulfonamidophosphoric acid. A solution of 0.005 mole of (II) in 10 ml of benzene was placed in a desiccator with a beaker of water. After a week, the product was filtered off and dried in

a vacuum desiccator over P_2O_5. The yield was 88.0%. The product was dissolved in a mixture of ether and benzene and precipitated with petroleum ether. The m. p. was 135-136°.

Found %: N 4.64, 4.70. Equiv. after hydrolysis, 1.93, 1.96. $C_7H_7O_5NSPF$. Calculated %: N 4.49. Equiv. after hydrolysis, 2.0.

p-Fluoro- and m-trifluoromethylphenyl trialkoxyphosphazosulfones and triaroxyphosphazosulfones and the diesters of p-fluoro- and m-trifluoromethylphenylsulfonamidophosphoric acids. Trialkoxy and dialkoxy derivatives. A solution of 0.075 g-at. of sodium in the appropriate alcohol was added to a solution of 0.025 mole of the appropriate aryl trichlorophosphazosulfone in 25 ml of dry benzene at 0-5°. The reaction mixture was left to stand at room temperature for 30 minutes. The benzene layer was washed with water. The aqueous extract was acidified with hydrochloric acid. The next day the precipitated dialkyl ester was filtered off and recrystallized. The benzene solution was dried. The benzene was removed. The trialkoxy derivatives was recrystallized or distilled.

The dialkoxy derivatives were also obtained by adding 0.09 g-at. of sodium in the appropriate alcohol to a solution of 0.02 mole of aryl trichlorophosphazosulfone in 25 ml of dry benzene. After 30 minutes, the mixture of benzene and salcohol was removed in vacuum. The residue was dissolved in water and the dialkyl ester precipitated by the addition of hydrochloric acid until the solution was acid to Congo.

Diaroxy and triaroxy derivatives. 0.06 g-at of sodium was added to a solution of 0.01 mole of aryl trichlorophosphazosulfone in 50 ml of benzene and to the boiling solution was added 0.06 mole of phenol in 40 ml of dioxane. The mixture was boiled until the whole of the sodium had reacted. The solution obtained was poured into a solution of 0.02 mole of aryl trichlorophosphazosulfone in 50 ml of benzene at 20°. The mixture was left for 1 hour. Further treatment was as in the case of trialkoxy derivatives.

p-Fluoro- and m-trifluoromethylphenyl trinitrotriphenoxyphosphazosulfones were prepared by boiling 0.01 mole of aryl trichlorophosphazosulfone with 0.03 mole of anhydrous sodium p-nitrophenolate in 25 ml of benzene for 20 hours. The product was extracted with boiling benzene. The benzene solution was filtered, part of the benzene evaporated and the solution left to crystallize.

Dinitrophenyl esters of p-flurophenyl and m-trifluoromethylphenylsulfonamidophosphoric acids were obtained by saponification of the trinitrophenyl esters by boiling with an aqueous alcohol solution of sodium carbonate and subsequent acidification of the solution obtained with hydrochloric acid.

SUMMARY

1. p-Fluoro- and m-trifluoromethylphenyl trichlorophosphazosulfones and their hydrolysis products were prepared.

2. Syntheses are described for 9 p-fluoro- and m-trifluoromethylphenyl trialkoxyphosphazosulfones and triaroxyphosphazosulfones and for 9 diesters of p-fluoro- and m-trifluoromethylphenylsulfonamidophosphoric acids for the purpose of studying their insectide properties.

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DERIVATIVES OF ETHYLENEIMINE

L ETHYLENEIMIDES OF PHOSPHORIC ACID

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Derivatives of phosphoric acid find application not only in agriculture (insecticides) and in industry, but also in medicine. Beginning in 1951, a series of articles has been published in the medical literature on a study of the action of some ethyleneimidies of phosphoric acids in the case of malignant neoformations. Two of these compounds, (A) and (B) underwent an extensive clinical study and
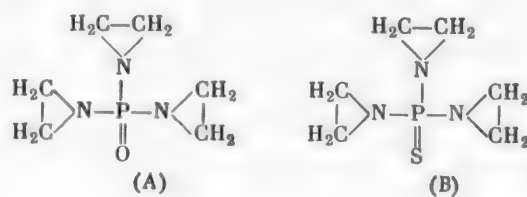
have found application in medical practice.

In 1955, we began work on the synthesis of ethyleneimino derivatives of phosphoric acid. It was proposed to synthesize compounds of the general formula
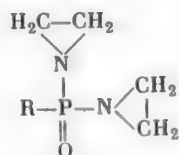
which contained 2 ethyleneimine rings and where various amino compounds were introduced as the third substituent R with the formation of a new N–P bond. In addition, it was found advantageous to synthesize some compounds in which aryloxy groups were introduced as the third substituent (R). The substance obtained were intended for a biological study to determine the effect of introducing different substituents R on the anticancer activity. The chemical literature contains several reports on ethyleneimine derivatives of phosphoric acid, though these are mainly patents [1].

The first part of the present work was the preparation of aryl-di(ethylene)-phosphorotriamides of the general formula

where

$$R = C_6H_5, \ p\text{-}ClC_6H_4, \ p\text{-}IC_6H_4, \ m\text{-}O_2NC_6H_4, \ p\text{-}CH_3OC_6H_4, \ p\text{-}H_5C_2OOCC_6H_4,$$

$$m\text{-}C_6H_4CON\!\!\begin{array}{c} CH_2 \\ | \\ CH_2 \end{array}, \ C_{10}H_7$$
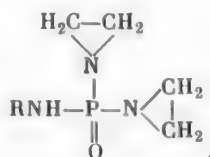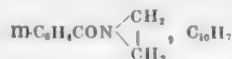
The following scheme was used for the preparation of these compounds:

$$RNH_2 \xrightarrow{POCl_3} \underset{(II)}{\underset{\underset{O}{\|}}{RNHPCl_2}} \xrightarrow{HN\begin{array}{c} CH_2 \\ | \\ CH_2 \end{array}} \underset{(III)}{\underset{\underset{O}{\|}}{RNHP}}\!\!-\!\!N\begin{array}{c} CH_2 \\ | \\ CH_2 \end{array}$$

(I)   (II)   (III)

By this scheme, N-oxychlorophosphines of arylamines (II) were obtained from appropriate amino compounds (I) and then the residual chlorine atom was replaced by ethyleneimine (III).

The N-oxychlorophosphines (II) were obtained by two methods: 1) the action of 1 mole of phosphorus oxychloride on 2 moles of amino compound in an inert solvent and 2) boi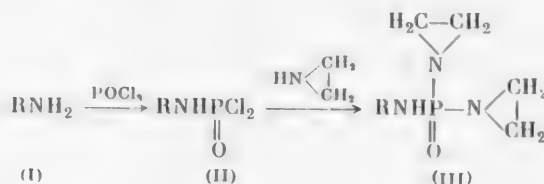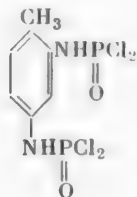ling the amino compound hydrochloride with excess phosphorus oxychloride. In all cases, freshly distilled phosphorus oxychloride was required. It was possible to obtain only the N-oxychlorophosphines of p-methoxyaniline and β-naphthylamine by the first method. All the other N-oxychlorophosphines (of aniline, p-chloroaniline, m-nitroaniline, m-aminobenzoyl chloride, p-iodoaniline and p-carbethoxyaniline) were obtained by the second method. The first four N-oxychlorophosphines of aniline were described previously by other authors [2]. Besides the N-oxychlorophosphines listed above, we also prepared the di-(N-oxychlorophosphine) of toluylenediamine, a compound with two N-oxychlorophosphine groups (No. 9, Table 1).

This compound also could only be prepared by boiling toluylenediamine dihydrochloride with phosphorus oxychloride. The N-oxychlorophosphines obtained and their properties are given in Table 1.

All the N-oxychlorophosphines obtained were treated with ethyleneimine to obtain the corresponding ethyleneimino derivatives. For this purpose we used Bestian's method [3], which consists of treating the phosphorus halide with ethyleneimine in benzene solution in the presence of triethylamine. By this method, we were able to replace the chlorine in all the N-oxychlorophosphines we obtained by the ethyleneimine ring. When the N-oxychlorophosphine of m-aminobenzoyl chloride (Table 1, No. 7) was treated with ethyleneimine, the halogen of the acid chloride group also reacted with ethyleneimine. According to literature data, the reaction of ethyleneimine with acid halides gives as the final reaction products, ethyleneimides, oxazoline derivatives and polymers. The compound that we obtained was not a polymer. According to elementary analysis data, this compound was either the ethyleneimide (IV) or the oxazoline derivative (V).

(No. 9, Table 1)
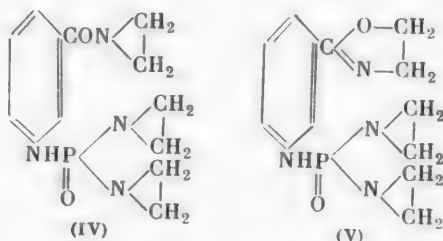
The problem of the structure of the compound obtained was resolved by means of the infrared spectrum. The presence of an absorption band at 1673 cm^{-1}, which is characteristic of an amide carbonyl group, in the infrared part of the spectrum, showed that the compound had structure (IV). * Thus, in this case a compound was obtained which had three ethyleneimine rings.

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*The spectra were plotted by Yu. N. Sheinker.

TABLE 1

$$\underset{\underset{O}{\parallel}}{RNHPCl_2}$$

Sample No.	R	M. p.	Yield (in %)	Recrystallization solvent	Chlorine content (in %)	
					found	calc.
1	C_6H_5	70°	42.7	Benzene	—	—
2	$p\text{-}ClC_6H_4$	103—104	74.3	Benzene	—	—
3	$p\text{-}IC_6H_4$	105—107	47.9	Benzene	21.14	21.11
4	$m\text{-}O_2NC_6H_4$	85—86	66.8	Benzene	—	—
5	$p\text{-}CH_3OC_6H_4$	71—72	41.3	Ether	29.40	29.48
6	$p\text{-}H_5C_2OOCC_6H_4$	100—102	68.8	Chloroform	25.12	25.06
7	$m\text{-}ClOCC_6H_4$	110 5—111.5	43	Chloroform	—	—
8	$C_{10}H_7$	115—116	83	Ether + chloroform	27.39	27.3
9	∗	153—154	53.5	Dioxane	40.00	39.87

∗See formula in text.

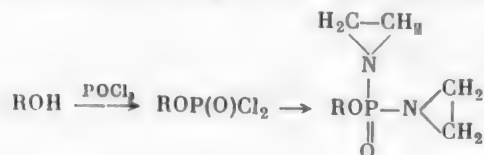The phenoxy compounds were obtained according to the following scheme:

$$ROH \xrightarrow{POCl_3} ROP(O)Cl_2 \rightarrow ROP-N\Big\langle\begin{smallmatrix}CH_2\\CH_2\end{smallmatrix}$$

TABLE 2

$$\underset{\underset{O}{\parallel}}{X-P}\left(N{<}^{CH_2}_{CH_2}\right)_2$$

Sample No.	X	M. p.	Yield (in %)	Recrystalliza- tion solvent	Found (in %)			Calc. (in %)		
					C	H	N	C	H	N
1	C_6H_5NH	143—144°	5.06	Benzene	53.57	6.26	18.82	53.80	6.32	18.82
2	$p\text{-}ClC_6H_4NH$	170—171.5	27.47	Benzene	46.64	5.08	16.20	46.61	5.08	16.30
3	$p\text{-}IC_6H_4NH$	176—177	77.07	Benzene	—	—	11.93	—	—	12.03
4	$m\text{-}O_2NC_6H_4NH$	166—167	57.2	Benzene	44.87	4.92	20.86	44.77	4.89	20.88
5	$p\text{-}CH_3OC_6H_4NH$	102—103	54.5	Benzene + petroleum ether	52.42	6.31	16.49	52.16	6.36	16.59
6	$p\text{-}H_5C_2OOCC_6H_4NH$	151—152	71.7	Benzene	52.89	6.09	14.08	52.80	6.14	14.2
7	$m\text{-}\overset{H_3C}{\underset{H_3C}{\diagdown}}NOCC_6H_4NH$	131—132.5	82	Benzene	53.36	5.80	19.05	53.41	5.86	19.17
8	$C_{10}H_7NH$	148	38	Benzene	61.33	5.82	15.62	61.5	5.85	15.45
9	∗	205—206 On heating to 200° in instrument	55.9	Dioxane	46.81	6.30	—	47.11	6.32	—
10	C_6H_5O	58—59	80	Petroleum ether + ethyl ether	53.08	5.80	12.40	53.56	5.84	12.49
11	$p\text{-}O_2NC_6H_4O$	73.5—74	64	Petroleum ether + ethyl ether	44.35	4.49	—	44.61	4.49	—

∗Ethyleneimino derivative, obtained from No. 9, Table 1.

By this scheme, treatment of the appropriate phenol with phosphorus oxychloride by Kraft's method yielded the acid chlorides of the phenyl ester and the p-nitrophenyl ester of phosphoric acid. The latter reacted with ethyleneimine to from the corresponding ethyleneimino derivatives (Table 2, Nos. 10 and 11).

Preliminary data on the biological properties of the compounds obtained were published in 1956 [4]. The results of more detailed biological tests will be published separately.

The authors are very grateful to the laboratory director Prof. S. L. Sergievskaya for showing interest in the work.

Z. D. Klyuchereva participated in the work.

EXPERIMENTAL

L. Preparation of N-oxychlorophosphines. N-Oxychlorophospine of β-naphthylamine. 25 g (0.017 mole) of β-naphthylamine in 400 ml of absolute ether was added with stirring and cooling (0—+5°) to 14.3 g (0.09 mole) of phosphorus oxychloride in 100 ml of absolute ether. After the addition, the reaction mixture was stirred for 1 hour with cooling and for 3 hours at room temperature. Then the β-naphthylamine hydrochloride was filtered off and the ether evaporated from the filtrate. The residue was recrystallized from a mixture of ether and benzene. The yield was 12 g (52.8%). The m. p. was 115-117° (with rapid heating).

The N-oxychlorophosphine of p-methoxyaniline was also prepared by the same method.

N-Oxychlorophosphine of p-carbethoxyaniline. 10.05 g (0.05 mole) of p-carbethoxyaniline (the ethyl ester of p-aminobenzoic acid) hydrochloride was added to 22.95 g (0.15 mole) of phosphorus oxychloride at room temperature. The reaction mixture was gradually heated until the oxychloride boiled and boiled until the whole of the oxychloride had dissolved. The excess phosphorus oxychloride was then distilled off under reduced pressure and the residue recrystallized from dry chloroform. Two recrystallizations yielded 9.94 g (68.18%) of substance. The m. p. was 100-102°.

This method was used to prepare the N-oxychlorophosphines of aniline, chloroaniline, iodoaniline, m-nitroaniline and m-aminobenzoic acid. The di-(N-oxychlorophosphine) of toluylenediamine was prepared in the same way with the only difference that 6 moles of phosphorus oxychloride were used per mole of diamine.

II. Preparation of ethyleneimino derivatives. With stirring and cooling (6-8°), a solution of 8.39 g (0.04 mole) of the N-oxychlorophosphine of aniline in 150 ml of absolute benzene was added from a dropping funnel to a solution of 3.44 g (0.08 mole) of ethyleneimine and 8.08 g (0.08 mole) of triethylamine in 120 ml of absolute benzene. As the solution was added, a precipitate of triethylamine hydrochloride formed. After the addition, stirring was continued at room temperature for a further 4 hours and the reaction mixture left until the next day. The triethylamine hydrochloride was then filtered off and the benzene distilled from the filtrate under reduced pressure. The residue was recrystallized twice from benzene. We obtained a colorless substance with m. p. 143-144° (4.5 g; 50.6%). All the other ethyleneimino derivatives were obtained in a similar way. The data are presented in Table 2 (Nos. 1-9).

Preparation of the phenyl ester of the bis-(diethyleneimide) of phosphoric acid. Over a period of 50 minutes, 4.22 g (0.22 mole) of the phenyl ester of the diacid chloride of phosphoric acid in 15 ml of absolute benzene was added with stirring to a solution of 1.72 g (0.04 mole) of ethyleneimine and 4.04 g (0.04 mole) of triethylamine in 20 ml of absolute benzene at 6-8°. After the addition, stirring was continued for a further 4-5 hours at room temperature and the reaction mixture left until the following day. The triethylamine hydrochloride was then filtered off, the precipitate was washed with dry benzene. The benzene solutions were combined and the benzene evaporated. Removal of the solvent left an oil, which crystallized on standing. The substance was washed several times with petroleum ether (60-80°). The yield was 3.65 g (about 80%) and the m.p. 55-57°. Recrystallization from a mixture of ethyl and petroleum ether yielded 2 g of material with m. p. 58-59°. The p-nitrophenyl ester of the bis-(diethyleneamide) of phosphoric acid was obtained in the same way. The data are presented in Table 2 (Nos. 10 and 11).

SUMMARY

1. 5 previously unreported N-oxychlorophosphines of arylamines were prepared.

2. 9 previously unreported di-(ethylene)-aryl-triamides of phosphoric acid and 2-phenyl esters of the di-(ethylene)-diamide of phosphoric acid were prepared.

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*Original Russian pagination. See C.B. Translation.

RULES GOVERNING THE CHANGES IN ACIDITY AND BASICITY IN AN HOMOLOGOUS SERIES OF α,ω-BIFUNCTIONAL COMPOUNDS

II. RULES GOVERNING THE CHANGES IN BASICITY OF SOME HOMOLOGOUS SERIES OF PRIMARY AMINES

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As is known, the basicity of amines is due to the presence of the unshared pair of p-electrons of the nitrogen atom and is determined by the degree of participation of this electron pair in the electron system of the adjacent and more distant bonds of the molecule or of other molecules, for example, of the solvent. Thus, for example, the low basicity of aromatic amines (aniline pK = 4.58, α-naphthylamine pK = 3.88, β-naphthylamine pK = 4.19 and 9-aminophenanthrene pK = 3.57) in comparison with that of aliphatic ones (pK = about 10.6) is produced by conjugation of the unshared p-electron pair with the π-electron system of the aromatic ring. With an increase in the distance between the amino group and the aromatic nucleus, their intereffect is reduced and this is accompanied by a gradual increase in the molecule's basicity.

Thus, the rules governing the change in basicity of an homologous series $X(CH_2)_nNH_2$, reflect the decrease in the interaction of the two electron systems in the molecule and are therefore quite interesting. However, the functional relation of basicity to the length of the chain was unknown up to the present time. In this work the rules governing the changes in basicity in the homologous series of ω-phenylalkylamines, aliphatic α,ω-n-diamines, aliphatic primary amines and cycloalkylamines were studied.

In accordance with Bronsted's concept, the basicity of the amines is characterized by the acidity index pK = $-$lg K of the appropriate ammonium ions; K is the equilibrium constant.

$$BH^+ + H_2O \rightleftarrows B + H_3O^+$$

1. ω-Phenylalkylamines $C_6H_5(CH_2)_nNH_2$. The acidity indexes of ω-phenylalkylammonium ions may be calculated with great accuracy from the equation

$$pK = \frac{\alpha n + \beta}{n + 1},$$ (1)

where $\alpha = 11.10$, $\beta = 7.60$ (Table 1)

The graph of (1) is a sigmoid which slowly straightens out (Fig. 1).

The pK values of ω-phenylalkylammonium ions may be calculated with the same accuracy by a similar equation for the function pK(v), where $\underline{v}$ is the number of C–C and C–N bonds [1]. With an increase in the length of the chain separating the aromatic ring and the amino group, the basicity of the ω-phenylalkylamines thus tends toward a definite limit of pK $\approx$ 11, which apparently corresponds to the limit of the basicity of aliphatic n-amines with a long chain.

One or two CH_3 groups at the C atom which is directly attached to the aromatic ring noticeably increase the basicity of the amine, apparently due to the competing conjugation of the CH_3 group with the π-electron system of the benzene ring [2].

TABLE 1

Acidity Indexes of ω-Phenylalkylammonium ions $C_6H_5(CH_2)_n\overset{+}{N}H_3$, Calculated by Equation (1)

n	pK	
	calculated	found experimentally (25°) [1]
1	9.35	9.34
2	9.93	9.93
3	10.22	10.22
4	10.40	10.40
5	10.52	10.52

TABLE 2

Acidity Indexes of Monoammonium Ions of Aliphatic n-α,ω-Diamines $H_2N(CH_2)_n\overset{+}{N}H_3$, Calculated by Equation (1)

n	pK	
	calculated	found experimentally (25°) [3,4]
2	9.93	9.93
3	10.40	10.54
4	10.68	10.71
5	10.87	10.86
6	11.00	10.93

One would expect that changes in basicity in the homologous series $CH_2 = CH - (CH_2)_n NH_2$, $CH \equiv C - (CH_2)_n NH_2$, $N \equiv C - (CH_2)_n NH_2$ would be analogous to changes in basicity in the ω-phenylalkylamine series. The basicity of the members of these series with $n > 1$ is unknown at the present time.
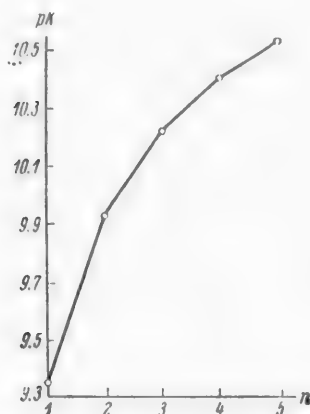

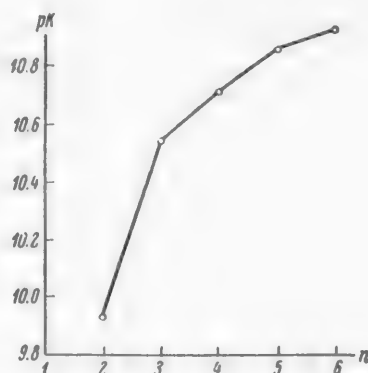Fig. 1. Relation of the acidity index of ω-phenylalkylammonium ions to the length of the carbon chain.

Fig. 2. Relation of the acidity of monoammonium ions of aliphatic n-α,ω-diamines to the length of the carbon chain.

It is interesting to compare the acidity indexes of the following ammonium ions: $CH_3CH_2CH_2CH_2\overset{+}{N}H_3$ 10.61, $CH_2 = CH - CH_2\overset{+}{N}H_3$ 9.53, $C_6H_5CH_2\overset{+}{N}H_3$ 9.34, $CH \equiv C - CH_2 - \overset{+}{N}H_3$ 8.15.

2. Aliphatic n-α,ω-diamines. The constant of the second dissociation stage $H_2N(CH_2)_n\overset{+}{N}H_3 + H_2O \rightleftharpoons H_2N(CH_2)_nNH_2 + H_3\overset{+}{O}$ is taken as the measure of basicity of members of this series. The law of changes in basicity in the series of aliphatic n-α,ω-diamines is the same as for ω-phenylalklamines (Fig. 2) except that the constants α and β have different values ($\alpha = 11.8$, $\beta = 6.2$) (Table 2).

As the distance between the amino groups increases, the acidity of the ion thus approaches the acidity of

a monoamine ion with a long chain (pK ≈ 11). With an increase in the length of the chain, the thermodynamic functions of diamine dissociation increasingly approach the corresponding values for monoamines with the same chain length [4]. Calculation by equation (1) for methylene diamine ($n = 1$) gives pK = 9.0. •

The similarity in the laws governing the increase in basicity with an increase in the distance between the amino group and the second terminal amino group or aromatic ring indicates that the mutual effect of these two electron systems are similar. The factors affecting the dissociation of mono- and diammonium ions of aliphatic n-α,ω-diamines were studied thoroughly by Everett and Pinsent [4].
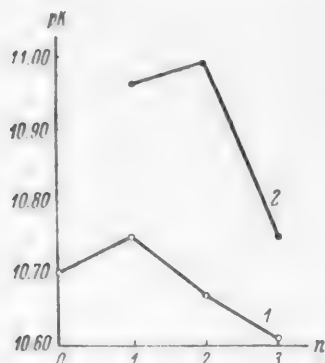
Fig. 3. The relation of the acidity index of primary aliphatic monoammonium (1) and trimethylsilyl-alkylammonium ions (2) to the length of the carbon chain.
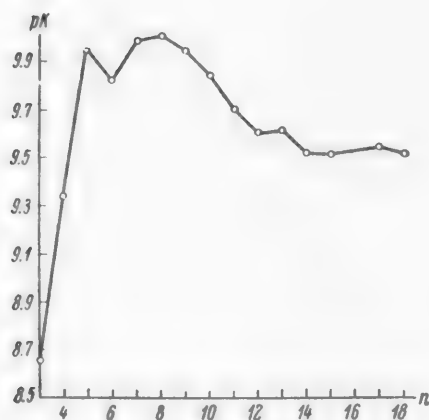
Fig. 4. The relation of the acidity index of cycloalkylammonium ions to the number of members in the ring.

TABLE 3

Acidity Indexes of Cycloalkylammonium Ions $(CH_2)_{n-1}CH\overset{+}{N}H_3$, Calculated by Equations (2-4)

n	pK	
	calc.	found experimentally (25°) [7,8]••
3	8.66	8.66
4	9.31	9.34
5	9.96	9.95
6	9.79	9.82
7	9.98	9.99
8	10.04	10.01
9	9.98	9.95
10	9.85	9.85
11	9.70	9.71
12	9.65	9.62
13	9.61	9.63
14	9.57	9.54
15	9.53	9.54

3. Primary aliphatic n-monoamines $CH_3(CH_2)_nNH_2$. At the present time it is difficult to define the character of the function pK(n) in the series of aliphatic n-monoamines as the basicity constants of the members of this series with $n > 3$ are unknown and differences in basicity in this series are quite small (Fig. 3). In our opinion, the noticeable decrease in basicity at $n = 2$ and especially at $n = 3$ could be due to a steric factor (disappearance of the blocking steric effect of the CH_3 group ?), which facilitates hydration of the amino group. In this case, the basicity of the amines should remain practically unchanged with a further increase in the length of the carbon chain as the steric factor remains almost unchanged. There are indications that the thermodynamic

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•Methylene diamine is stable only in the form of salts, which are readily hydrolyzed in solution to form formaldehyde.
••The pK values for cyclopropyl-, cyclobutyl-, cyclopentyl- and cyclohexylamine were obtained electrometrically in 50% ethanol [7] and for members of the same series with $n = 6$-15 in 80% cellosolve solution [8]. We consider that the data from these two series of measurements may be compared as cyclohexylamine had the same pK value in the two cases. In all probability the character of the change in basicity of the amine was retained in going from one solvent to the other [9].

functions of the dissociation of primary ammonium ions approach constant limits with an increasing chain length [5]. It is interesting that there is an even more noticeable decrease in basicity for the member with n = 3 of the trimethylsilylalkylamine series $(CH_3)_3Si(CH_2)_nNH_2$ [6] (Fig. 3). The basicity of γ-trimethylsilyl-amine, which is noticeably greater than that of n-propylamine, at the same time excludes coordination of the unshared electron pair of the nitrogen with the Si atom with the expansion of the valence shell of the latter [6].

4. Cycloalkylamines $(CH_2)_{n-1}CH-NH_2$. The differences in basicity are small in the homologous series of the cycloalkylamines. The pK(n) function is quite complex in this series (Fig. 4). There are two outstanding maxima, one for n = 5 and the other in the region n = 7, 8 and 9. Accurate equations may be given only for separate regions (Table 3).

$$\text{For } n = 3-5 : pK = 0.65n + 6.71, \tag{2}$$

$$\text{for } n = 6-10 : pK = 16 \lg n - 0.87n + 2.55, \tag{3}$$

$$\text{for } n = 11-15 : pK = 11 - 1.25 \lg n. \tag{4}$$

Cycloalkylamines are weaker bases than the corresponding aliphatic amines. The basicity of an amino group is thus decreased not only by the immediate proximity of an aromatic ring, but also apparently by any other ring. This indicates a greater or lesser participation of the unshared pair of nitrogen p-electrons in the electron system of the ring. In our opinion, the differences observed in the basicity of cyclic amines may be due to the different degree of "compactness" of the electron system, which is related to the different degree of coplanarity of multimembered rings.

SUMMARY

The rules governing the changes in basicity in the homologous series of ω-phenylalkylamines, aliphatic α,ω-n-diamines and cycloalkylamines were established; empirical equations for the pK(n) functions for these series are put forward.

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OXIDATION-REDUCTION SYSTEMS FOR THE INITIATION OF RADICAL PROCESSES

IX. THE MECHANISM AND EFFICIENCY OF THE ACTION OF POLYAMINE SYSTEMS IN POLYMERIZATION

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All the known oxidation-reduction systems used for initiating radical processes may be divided into two types according to the mechanism of their action. The first, more common type, consists of systems which act through metals of variable valence. Reaction in such systems always results in the formation of one radical

$$Me^n + BX \rightarrow Me^{n+1} + B\cdot + X^-$$
$$Me^{n+1} + AH \rightarrow Me^n + A\cdot + H^+,$$

where BX is the oxidant and AN the reductant.

The second type consists of systems in which the oxidation-reduction reaction leads to the formation of two radicals, for example:

$$ROOH + AH \rightarrow RO\cdot + H_2O + A\cdot$$
$$SO_2 + C_6H_2Cl_3SH \rightarrow (\cdot SO_2H) + C_6H_2Cl_3S\cdot$$

In both types of system the free radicals are formed directly in the stage of the oxidation-reduction reaction.

Systems in which hydroperoxides and polyethylenepolyamines participate belong to a new type of system which, as the present investigation showed, is characterized by a primary oxidation-reduction reaction leading to the formation of a new intermediate compound, which is thermally unstable and decomposes into radicals at a lower temperature than the starting hydroperoxide.

Papers [1 and 2] showed that systems consisting of hydroperoxides and polyethylenepolyamines, in which the amino groups are separated by two carbon atoms ($>N-CH_2-CH_2-N<$), are extremely efficient in initiating polymerization in emulsions at low temperatures. In the polyethylenepolyamine series, tetraethylenepentamine and pentaethylenehexamine are the most efficient. Many authors have established [3-6] that the activity of these systems is considerably increased in the presence of small amounts of iron salts due to the increase in the reaction rate of the oxidant with the reductant. The maximum polymerization rate was attained by using the hydroperoxides of tert -butylisopropylbenzene, tetraethylenepentamine and a small amount of ferric naphthenate [7]. In the latter case a 60% degree of polymerization was attained in 2 hours at a temperature of $+5°$.

In spite of the wide use of polyamine systems for the initiation of polymerization at low temperatures [8], up to now the mechanism of their action has not been elucidated. One of us and Korotkina showed [7] that at $0°$ polyamines do not reduce Fe^{3+} to Fe^{2+} and this excluded the possibility of the process developing by a mech-

anism of reversible systems. It was proposed that the hydroperoxide decomposed rapidly due to the catalytic effect of a complex formed from the polyamine and iron salts. Orr and Williams [9 and 10] came to the same conclusions when studying the kinetics of the reaction of polyamines with the hydroperoxides of isopropylbenzene and tert -butylisopropylbenzene in the presence of Fe^{2+} salts.

To explain the mechanism of the initiating action of polyamine systems, various proposals based on the hypothesis that the free radicals are formed directly in the stage of the oxidation-reduction reaction have been put forward:

1. a) $(RNH_2Fe^{2+}) + R_1OOH \rightarrow R_1O\cdot + OH^- + (RNH_2Fe^{3+})$,
   b) $(RNH_2Fe^{3+}) + R_1OO^- \rightarrow R_1OO\cdot + (RNH_2Fe^{2+})$;

2. $(RNH_2Fe^{2+}) + R_1OOH \rightarrow R_1O\cdot + RNH + H_2O + Fe^{2+}$;

3. $(RNH_2Fe^{3+}) + R_1OOH \rightarrow R_1O\cdot + RNH + H_2O + Fe^{3+}$

Scheme 1 [10] provides for the catalytic action of the complex of the amine and Fe^{2+} salts, with the free radicals arising only from the hydroperoxide. Scheme 2 [25] is based on the hypothesis that during the oxidation-reduction reaction with catalytic participation of Fe^{2+} salts, the radicals are formed from the hydroperoxide and polyamine. In scheme 3 [7] the same role is played by ferric salts.
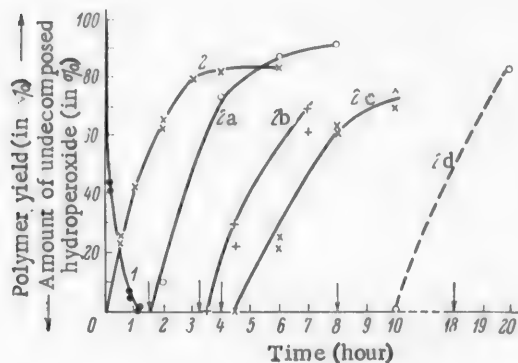

Fig. 1. Kinetics of polymerization and consumption of hydroperoxide. 1) Kinetics of hydroperoxide decomposition, 2, 2a, 2b, 2c and 2d—kinetics of polymerization (explanation in text). The arrow indicates the moment of introduction of styrene.
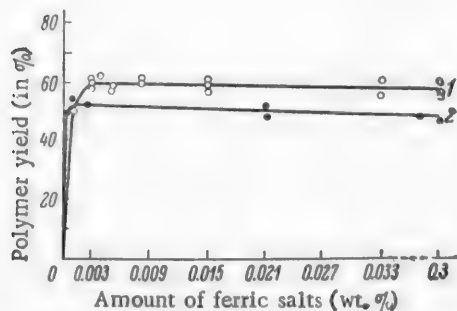

Fig. 2. The effect of ferric salt concentration on the polymerization rate (polymer yield in 2 hours at 5°). 1) Ferric naphthenate, 2) $Fe_2(SO_4)_3$.

From the above ideas one would expect the presence of a definite symbatic relation between the kinetics of hydroperoxide decomposition in the system and the initiating effect during polymerization. However, our investigation showed the absence of a kinetic relation between the reaction of the hydroperoxide with the polyamine and polymerization. In Fig. 1, curve 1 shows the kinetics of tert -butylisopropylbenzene hydroperoxide consumption when the latter reacts with tetraethylenepentamine in the presence of Fe^{3+} naphthenate at 5° in a water-ethylbenzene emulsion. Curve 2 illustrates the kinetics of styrene polymerization under these conditions. However, if hydroperoxide was decomposed completely under the same conditions in a water-ethylbenzene emulsion and then styrene was introduced into the system after different time intervals, then the polymerization after a certain induction period proceeded at the same rate as in the presence of all the components of the system (curves 2a, 2b, 2c and 2d). Polymerization did not proceed only when the styrene was introduced 18 hours after the complete consumption of the hydroperoxide. The same phenomenon was observed when methylmethacrylate was introduced into the system after the complete consumption of the hydroperoxide when the reaction was carried out in an aqueous medium. It follows from this that initiation of polymerization is directly connected with the formation of some new intermediate products which gradually decompose to form free radicals, and not with the reaction of the hydroperoxide with the amine. Similar results were obtained in studying the reaction mechanism of an ethylenediamine-hydroperoxide system [1].

It was established previously that the decomposition rate of isopropylbenzene hydroperoxide increased

considerably with an increase in the concentration of ferric salts in the system [7]. However, as Fig. 2 shows, the polymerization rate hardly depends on the content of ferric salts. The absence of a connection between the kinetics of hydroperoxide decomposition and the polymerization kinetics in this case agree with the idea put forward that polymerization initiation is not related to the stage of hydroperoxide decomposition.

In order to clarify the nature of the intermediate compounds we studied the reaction products of triethylenetetramine with isopropylbenzene hydroperoxide with and without monomers as acceptors of the free radicals formed. The reaction was carried out in an aqueous medium in the presence of an iron pyrophosphate complex and in a hydrocarbon medium in the presence of ferric naphthenate. By carrying out the process in water with methylmethacrylate and in a hydrocarbon medium with α-methystyrene it was established that the primary amino groups were not consumed in the reaction (Table 1). The method used was based on the capacity of primary amines to give a violet color when reacted with ninhydrin, the color intensity increasing with an increase in amine concentration [17].
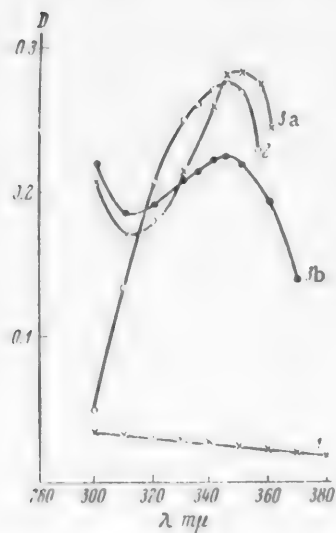

Fig. 3. Absorption spectra. 1) 1% solution of triethylenetetramine, 2) 1% solution of dimethylnitrosamine, 3a and 3b) aqueous extract of reaction products.

In order to establish the degree to which the secondary amine groups participated in the reaction we studied the reaction of isopropylbenzene hydroperoxide with triethylenetetramine in a solution of ethylbenzene in the presence of nitric oxide, which, as is known, adds readily to free radicals to form nitroso compounds. If the $\frac{R}{R}{>}N\cdot$ type of radical were formed in the reaction one would expect the formation of nitrosamines. The actual formation of the latter was established by studying the absorption spectra of the reaction mixture in the ultraviolet region. It is known from literature data [18] that the absorption spectra of nitrosamines in the ultraviolet region have characteristic absorption maxima at 330-350 cm^{-1}. The absorption curves we obtained for dimethylnitrosamine and for the aqueous extracts of the reaction mixture showed maxima in the region 340-350 cm^{-1}, caused by the presence of $>N-NO$ groups (Fig. 3). The formation of nitrosamines in the presence of nitrogen oxide is direct proof of the formation of the $\frac{R}{R}{>}N\cdot$ type of free radical. The formation of nitrogen-containing radicals was also proved by establishing the presence of nitrogen in the polymethylmethacrylate chain in polymerization in the presence of a polyamine system.

The reaction mechanism of isopropylbenzene hydroperoxide with triethylenetetramine and further conversion of the decomposition products may be represented by the following scheme:

$$R = NH_2-CH_2-CH_2$$
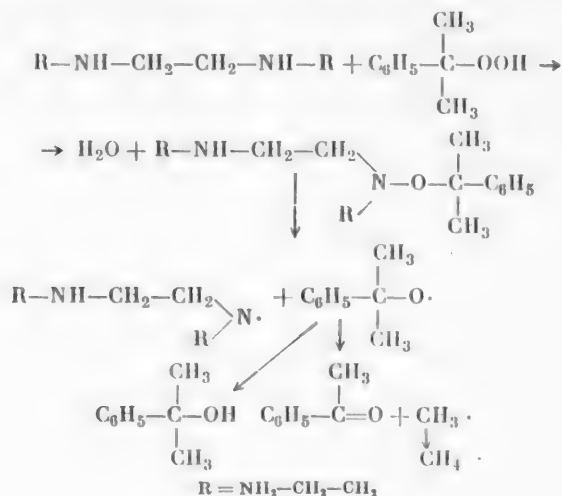
In the first stage the reaction results in the formation of an intermediate compound, containing an un-stable N-O bond. The formation of water at this stage was proved experimentally by carrying out the reaction in α-methylstyrene. In this case after the hydroperoxide had been decomposed completely, 80-84% of the theoretical amount of water was found. The formation of free radicals is connected with the thermal dissocia-tion of primary reaction products at the N-O bond.

TABLE 1

Consumption of Primary Amino Groups in the Reaction of Hydro-peroxide with Triethylenetetramine at 20°

Molar ratio of hydroperoxide : amine = 12 : 1 (2 hydroperoxide molecules per N-H bond)

Experimental conditions	Time (in hours)	Amount (in %)	
		hydro-peroxide	triethylenetetra-mine (calc. on primary amino groups)
Aqueous solution without monomer	0	100	100
	0.5	94.5	95.5
	2	86.0	100
	4	82.5	101
In an α-methyl-styrene solution	0	100	100
	0	100	100
	0	100	100
	1.5	37.3	104.0
	1.5	37.3	104.5
	1.5	37.3	104.0

The formation of intermediate compounds, containing N-O bonds, in the reaction of aliphatic-aromatic amines with benzoyl peroxide had been previously demonstrated by Gambar'yan et al. [12] and by Horner [14, 15, 23]. The authors assigned structure (A) to this compound.

$$C_6H_5-\underset{\underset{(A)}{}}{\overset{\overset{O}{\|}}{C}}-O-N\underset{R}{\overset{R}{<}}$$
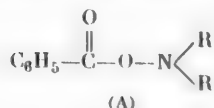
These results were confirmed in paper [13], which showed that in the case when benzoyl peroxide reacted with dimethylaniline the main reaction product, benzoic acid was also formed after complete decomposition of the peroxide. According to the authors, this fact indicates the formation in the first stage of a relatively unstable compound which slowly decomposes with the liberation of benzoic acid.

The scheme given above for the reaction of hydroperoxide with polyamines was also confirmed by the composition of the final reaction products. The process, when carried out in an aqueous medium in the presence

TABLE 2

Composition of the Reaction Products of Isopropylbenzene Hydro-peroxide with Triethylenetetramine in an Aqueous Medium

Reaction products	Amount (in % of hydroperoxide consumed)	
	20°	70°
Dimethylphenyl-carbinol	59.3, 61.5	67.8, 71.5
Acetophenone	37.6, 37.4	22.4, 21.7
Methane	23.4, 23.2	24.1, 25.1

of an iron pyrophosphate complex, gave acetophenone, dimethylphenylcarbinol and methane in the quantities shown in Table 2.

It follows from the quantitative data given that dimethylphenylcarbinol, acetophenone and methane are the main final reaction products and their formation agrees with the scheme given above.

Thermal dissociation of the primary reaction product led to the formation of two radicals with reaction centers at the nitrogen atoms in one of them and at the oxygen atom in the other. The formation of carbinol was due to the elimination of hydrogen in the reaction of the RO • radical with the amine. The formation of acetophenone and methane was due to decompoistion of the RO • radical. Methane was evolved both during the decomposition of hydroperoxide and after it had been consumed completely, with the evolution increasing with an increase in temperature. Figure 4 illustrates the kinetics of methane evolution at + 5°. The kinetics of methane evolution after complete consumption of the hydroperoxide is in agreement with the capacity of the system to retain its activity for polymerization initiation.
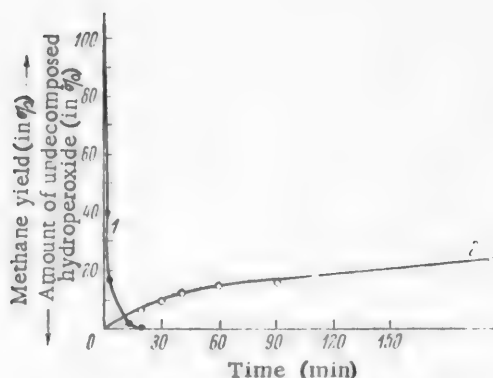

Γig. 4. Kinetics of hydroperoxide decomposition and methane evolution. 1) Hydroperoxide decomposition, 2) methane yield (in %).

Fig. 5. The effect of the amount of hydroperoxide on the reaction rate at 20°. 1) Molar ratio of hydroperoxide to amine 1 : 24, 2) 1 : 12, 3) 1 : 9, 4) 1 : 24 (1,2,3 — in a α-methylstyrene solution, 4 — in an ethylbenzene solution).

A study of the composition of the product formed in the presence of unsaturated monomers, capable of "picking up" the starting active centers, was particularly interesting. When the reaction of isopropylbenzene hydroperoxide with triethylenetetramine was carried out in an aqueous solution in the presence of methylmethacrylate as well as in a solution of α-methylstyrene no methane was evolved and the amount of carbinol fell noticeably which is further confirmation of the scheme given above for the formation of methane and carbinol (Table 3). The yield of acetophenone even increased somewhat under these conditions. This fact is a direct indication that the formation of acetophenone in this case is not related to the radical stages of the process. This hypothesis is also confirmed by the fact that when the process was carried out at + 20° without free radical acceptors, the acetophenone yield was considerably greater than the methane yield (see Table 2), while the above scheme provides for an equimolecular yield of the given product. It is possible that acetophenone was also formed directly by decomposition of the intermediate compound, for example by scheme:

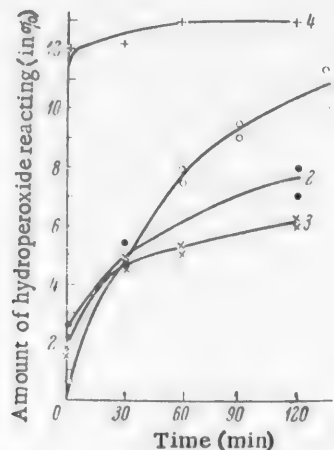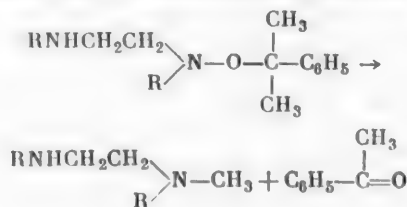$$\begin{array}{c} RNHCH_2CH_2 \\ \diagdown \\ R \end{array} N-O-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-C_6H_5 \rightarrow$$

$$\begin{array}{c} RNHCH_2CH_2 \\ \diagdown \\ R \end{array} N-CH_3 + C_6H_5-\overset{\overset{CH_3}{|}}{C}=O$$

To determine the stoichiometry of the reaction we studied the reaction of triethylenetetramine with iso-propylbenzene hydroperoxide in a solution of α-methylstyrene in the presence of ferric naphthenate in a nitrogen medium. This established that at a constant amine concentration the amount of hydroperoxide moles consumed per amine molecule varied, depending on the starting concentration of hydroperoxide (Table 4).

TABLE 3

Composition of Reaction Products of Iso-propylbenzene Hydroperoxide and Tri-ethylenetetramine in α-Methylstyrene at 20° (in % of consumed hydroperoxide)

Reaction product	Amount (in %)
Dimethylphenylcar-binol	39.1, 39.2
Acetophenone	49, 51
Methane	0
Water	79.8, 84.2

TABLE 4

The Relation of the Maximum Extent of Isopropyl-benzene Hydroperoxide Decomposition in a Reaction with Triethylenetetramine to Starting Concentration of Hydroperoxide in an α-Methylstyrene Solution (at 20°)

Molar ratio of amine and hydroperoxide in starting mixture	Weight concentration of hydroperoxide in the starting mixture (in %)	Maximum number of hydroperoxide moles reacting with one mole of polyamine
1 : 24	3	14.4, 15
1 : 12	1.5	9.1, 9.3
1 : 9	1.12	8.2, 8.5

The amount of hydroperoxide decomposed was considerably greater than the amount of N-H groups in the polyamine. Such an effect may be due either to a chain process for the hydroperoxide decomposition or to the participation of CH_2 groups in the polyamine in the interaction.
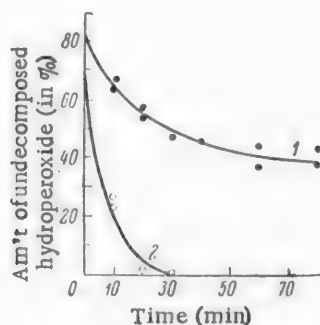
Fig. 6. The effect of nitrogen oxide on the reaction rate of isopropylbenzene hydroperoxide with triethylenetetramine in ethylbenzene with a molar ratio equal to 1. 1) In the presence of NO, 2) in the absence of NO.
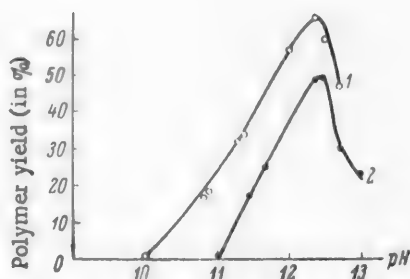
Fig. 7. The effect of medium pH on the rate of polymerization (polymer after 2 hours). 1) Ferric naphthenate, 2) $Fe_2(SO_4)_3$.

The reaction rate was considerably greater in an ethylbenzene solution than in α-methylstyrene (Fig. 5). The retardation of hydroperoxide decomposition in an α-methylstyrene solution in this case is, apparently, due to the formation by the reaction of the monomer with the primary radicals of tertiary radicals with low reactivity, which lower the contribution of the chain hydroperoxide decomposition process. As was shown [19] aliphatic radicals react with α-methylstyrene in the following way:

$$R\cdot + CH_2=\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-C_6H_5 \rightarrow R-CH_2-\underset{\underset{CH_3}{|}}{\overset{\overset{\cdot}{}}{C}}-C_6H_5 \rightarrow R-CH_2-CH-C_6H_5 + R-CH_2-\underset{\underset{CH_2}{||}}{C}-C_6H_5$$

TABLE 5

Composition of Polymerization Mixture (in parts by weight)

	I	II
Divinyl	70	70
Styrene	30	30
Water	250	240
Tert -butylisopropylbenzene hydroperoxide	0.4	0.3
Tetraethylenepentamine	0.6	0.4
Ferric naphthenate	0.005	—
Ferric sulfate	—	0.004
KOH	—	0.21
Potassium paraffinate	10	0.7
Sodium salt of dibutylnaphthalenesulfonic acid ("necal")	—	5.7
Sodium salt of the condensation product of naphthalene-sulfonic acid with formaldehyde ("leicanol")	0.25	0.5
Time to achieve 60% polymerization	30-50 min	4.5-5 min

The chain character of hydroperoxide decomposition was also confirmed by the decrease in the reaction rate and decrease in the amount of hydroperoxide decomposed in the presence of nitrogen oxide (Fig. 6).
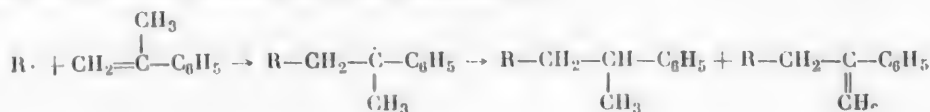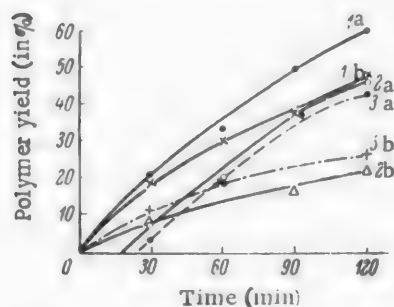

Fig. 8. The effect of various metal salts on the polymerization rate. 1a) Ferric naphthenate, 1b) $Fe_2(SO_4)_3$, 2a) lead naphthenate, 2b) $PbSO_4$, 3a) copper naphthenate, 3b) $CuSO_4$.
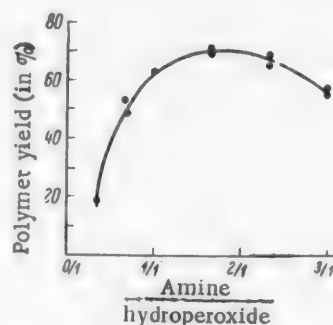
Fig. 9. The effect of the molar ratio of amine and hydroperoxide on the polymerization rate (2 hours duration of process).

The efficiency of the system for initiating polymerization in an emulsion at + 5°. In studying polymerization as affected by tert -butylisopropylbenzene hydroperoxide, tetraethylenepentamine and ferric naphthenate, it was shown that the pH of the medium and concentration of the emulsifiers had the greatest effect on the rate of the process. The maximum rate was attained in a very narrow range of pH (12.4-12.6) and in using potassium naphthenate as emulsifier (Fig. 7).

The system was most active when metal naphthenates, that are soluble in a hydrocarbon phase, are used. The naphthenates of various metals may be arranged in the following series according to their effect on the polymerization rate (Fig. 8): Fe > Cu > Pb > Cr. When metal sulfates are used the polymerization rate does not depend on the nature of the metal. The optimal molar ratios of amine to hydroperoxide were in the range from 1.7: 1 to 2.3:1 (Fig. 9). Under the optimal conditions at + 5° the required extent of polymerization (60%) may be achieved in 30-50 minutes (Table 5, I).. When "necal" was used as emulsifier, a 60% polymerization was reached in 4.5 to 5 hours at a "necal" concentration of 5.7% relative to the monomers (Table 5, II).

A characteristic of polyamine systems is their insensitivity   to oxygen, which has a strong inhibiting effect on polymerization in other systems. The inhibiting effect of oxygen is characteristic of systems in which phenols or aromatic amines participate and in systems in which polymerization initiation depends on ferrous salts.

Experimental Procedure

Starting materials. Triethylenetetramine: b. p. 119-120° (1 mm), n^{20}D 1.5015. The material was synthesized by von Alphen's method [20]. The isopropylbenzene hydroperoxide had a hydroperoxide content of 98%. The iron pyrophosphate complex had a ferric ammonium alum to sodium pyrophosphate ratio of 1 : 1.2.

The consumption of primary amino groups was determined by Moore and Stein's method [7], which was developed for α-amino acids.

Analysis of the reaction mixture for acetophenone. a) The acetophenone was isolated from the reaction mixture as the p-nitrophenylhydrazone and its identity established by a mixed melting point with an authentic sample. b) The acetophenone was determined quantitatively by a titrimetric and a gravimetric method [21].

Analysis of the mixture for dimethylphenylcarbinol. a) The presence of dimethylphenylcarbinol in the mixture was demonstrated by the absence of depression in a mixed melting point of a crystalline derivative obtained by reacting thioglycolic acid and dimethylphenylcarbinol with the crystalline derivative obtained from the reaction mixture. To prepare the crystalline derivative, 2 g of the substance examined was heated for 1 hour with 1 g of thioglycolic acid in 10 ml of 2 N HCl under reflux on a water bath. Then the reaction mixture was cooled and washed with water. The oil formed was extracted with a saturated KOH solution. The oil liberated on acidifying the alkaline extract crystallized on standing. After separation, washing and drying, the substance had m. p. 67° [22]. b) The dimethylphenylcarbinol was determined quantitatively by a titrimetric method [21]. c) In the reaction of hydroperoxide with polyamines in α-methylstyrene, the dimethylphenylcarbinol was determined quantitatively by Terent'ev and Shcherbakova's method [16]. After the reaction and before the determination of the amount of hydroxyl groups, the reaction mixture was washed with water to remove amines and dried with baked sodium sulfate to remove water. Water was shown to be absent from the mixture investigated by the Fischer method and amines were shown to be absent by a microanalysis for the nitrogen content of the mixture.

Reaction of isopropylbenzene hydroperoxide with triethylenetetramine in a nitric oxide medium. The reaction was run in hydrogenation flasks with constant stirring under   nitric oxide pressure or with nitric oxide bubbled through the mixture continuously. Before the reaction, the vessels were pumped out three times with subsequent filling with nitrogen and then with nitric oxide. After the reaction, the nitric oxide was flushed out with nitrogen and then samples removed for determination of the peroxide content. The presence of nitrosamines in the reaction mixture was established by extracting the latter with water and examining the aqueous extracts spectrophotometrically.

Polymerization of styrene. Tert -butylisopropylbenzene hydroperoxide and tetraethylenepentamine were reacted in the presence of ferric naphthenate in ampules in a nitrogen medium at + 5° in the following amounts (parts by weight): ethylbenzene 100, water 500, potassium paraffinate 10, styrene 100, polyamine 2.4 and hydroperoxide 0.65.

The styrene was introduced with an injector through a self-closing stopper after the complete consumption of the peroxide. The peroxide consumption was determined iodometrically. The yield of polystyrene was determined from the weight of polymer, isolated by coagulation of the latex with acetic acid, washing with water and methyl alcohol and drying in vacuum at 100°.

The water formed during the interaction of the hydroperoxide with the polyamine in a hydrocarbon medium (ethylbenzene and α-methylstyrene) was determined by Gulyaeva's method [24]. The determination is based on determining the volume of acetylene liberated during the reaction of calcium carbide with water.

The reaction was performed in an atmosphere of nitrogen in a reactor, into which the calcium carbide was introduced at the end of the reaction.

SUMMARY

1. It was shown that in its action mechanism, the *polyamine system* is a new type of system in which the initiation is not directly connected with the oxidation-reduction stage. The primary reaction product is a new compound, which dissociates into radicals at a lower temperature than the original hydroperoxide.

2. Data were obtained on the composition of the reaction products of the hydroperoxide and polyamines, which made it possible to consider the mechanism of the main and side reactions.

3. The possibility of using the *polyamine system* for establishing a high-efficiency polymerization process in emulsions at a temperature of + 5° was demonstrated.

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ABSORPTION SPECTRA AND STRUCTURE OF SUBSTITUTED QUINOLINES USED AS STARTING MATERIALS FOR ANTIMALARIALS

VI. THE INTERACTION OF SUBSTITUENTS IN IONS OF 8-AMINOQUINOLINE, 6-METHOXY-8-AMINOQUINOLINE AND SOME OF THEIR DERIVATIVES

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It was established in previous investigations [1, 2] that an unsubstituted ion of quinoline has an ultraviolet absorption spectrum similar to those of benzene derivatives with one electron-acceptor and one electron-donor substituent. The similarity in electronic structure of the quinoline ion to that of o-aminostyrene and o-aminoacetophenol was observed. One would expect that the ions of 8-aminoquinoline and 6-methoxy-8-aminoquinoline and some of their derivatives substituted at the amino group would behave as the corresponding benzene derivatives.

EXPERIMENTAL

6-Methoxy-8-aminoquinoline was prepared by reducing 6-methoxy-8-nitroquinoline according to the data in [3] and purified by vacuum distillation and recrystallization from a mixture of benzene and benzine. 8-Aminoquinoline was purified by vacuum distillation and recrystallization from heptane [4]. 8-(5'-Diethyl-amino-2'-pentyl)-aminoquinoline (neoplasmoquin) was synthesized according to data in [5] and purified by vacuum distillation. 6-Methoxy-8-(3'-diethylamino-1'-propyl)-aminoquinoline (plasmocide) was purified by vacuum distillation [6]. The hydrochloride of 6-methoxy-8-(4'-aminopentyl)-aminoquinoline (quinocide) was purified by recrystallization from anhydrous alcohol [7]. All the above materials had melting or boiling points which agreed with those in the literature.

The spectrographic investigation was carried over a concentration range of $2 \cdot 10^{-2} - 2 \cdot 10^{-5}$ M in sulfuric acid and in ethanol solutions of hydrogen chloride.

The absorption spectrum of an 8-aminoquinoline salt at the ring nitrogen is comparable with the spectra of ortho-derivatives of benzene which have one electron-acceptor and one electron-donor substituent in the ring; for example it was similar to the spectral curve of o-aminostyrene (Fig. 1, curves 2, 5 and 4). In accordance with this these bands of the 8-aminoquinoline ion have been provisionally called "o-aminostyrene" absorption bands. A third band with a fine structure and with maxima at λ equals 3140 and 3030 A was superimposed on this "o-aminostyrene" spectrum of two highly intense absorption bands. The origin of this third band in the spectrum of 8-aminoquindine ion was established by comparing it with a similar band (with a fine structure) in the benzimidazole spectrum or with the band of o-phenylenediamine [9] (Fig. 1, curves 1, 2 and 9), i.e., benzene derivatives which have two electron-donor substituents in the ring. On this basis, the corresponding band of 8-aminoquinoline ion was provisionally called an "o-phenylenediamine" absorption band.

With molar ratio of 8-aminoquinoline to hydrogen chloride to less than 1 : 500, salt formation at the ring nitrogen was incomplete and, in accordance with the equilibrium established, the band of the "o-benzene-pyridine" spectrum [8] corresponding to the base was noted on the absorption curves, superimposed on the bands

of the "o-aminostyrene-phenylenediamine" spectrum, which corresponded to the salt at the ring nitrogen. As a result of the superposition the 8-aminoquinoline ion has a complex spectrum of five absorption bands (Fig. 1, curves 1, 2 and 3).
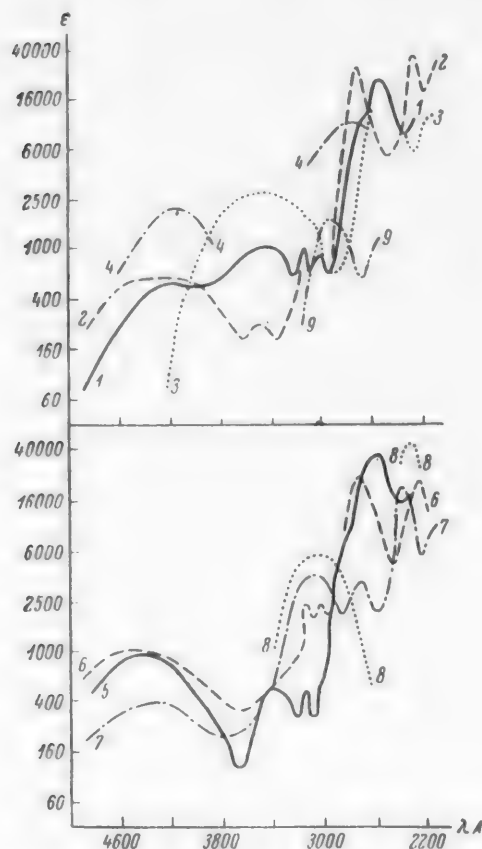
Fig. 1. Absorption spectra. 1) 8-Aminoquinoline in an ethanol solution of hydrogen chloride (molar ratio 1 : 10), 2) 8-aminoquinoline in ethanolic HCl solution (molar ratio 1 : 100), 3) 8-aminoquinoline in ethanol, 4) o-aminostyrene in ethanol according to data [12] (the long wavelength spectrum band is bathochromically displaced by 800 A and the short wavelength one by 400 A), 5) neoplasmoquin in an ethanolic HCl solution (molar ratio 1 : 1000), 6) 8-aminoquinoline in an ethanolic HCl solution (molar ratio 1 : 1000), 7) 8-aminoquinoline in 5 M ethanolic HCl solution, 8) quinoline in 5 M ethanolic HCl solution (part of curve), 9) o-phenylenediamine in ethanol according to data [14].
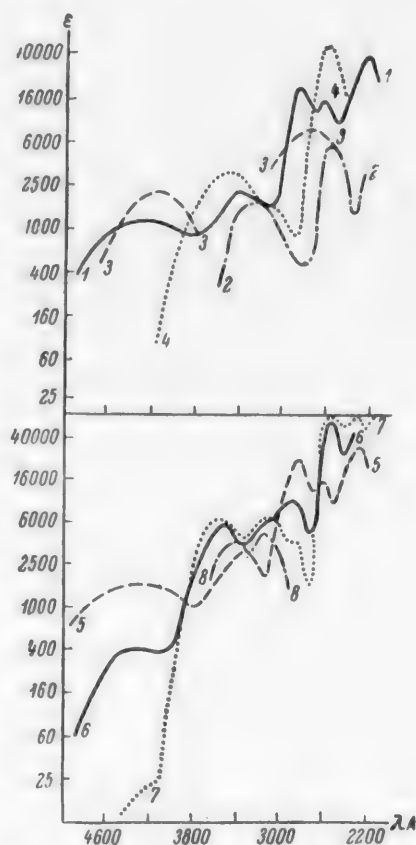
Fig. 2. Absorption spectra. 1) 6-Methoxy-8-aminoquinoline in an ethanolic HCl solution (molar ratio 1 : 100), 2) 2-hydroxybenzaldehyde, according to data [13], in an ethanolic HCl solution (molar ratio 1 : 200), 3) o-aminostyrene in ethanol, according to data [12] (the long wavelength spectrum band is displaced bathochromically by 800 A and the short wavelength by 400 A), 4) 6-methoxy-8-aminoquinoline in ethanol, 5) 6-methoxy-8-aminoquinoline in an ethanolic HCl solution (molar ratio 1 : 1000), 6) 6-methoxy-8-aminoquinoline in 4 M ethanolic HCl solution, 7) 6-methoxy-8-aminoquinoline in 5 M sulfuric acid, 8) 6-methoxy-quinoline in 5 M sulfuric acid (part of curve).

The diethylaminopentyl radical has little effect on the character of the absorption of the 8-aminoquinoline salt at the ring nitrogen (Fig. 1, curves 5 and 6).

More complex relations, comparable with those for a singly charged 8-aminoquinoline ion, were observed between the substituents in the 6-methoxy-8-aminoquinoline salt at the ring nitrogen. Besides the two "o-amino-

styrene* bands, which are characteristic of its singly charged ion, two other bands λ_{max} 3340 A, ϵ 24000 and λ_{max} 2590 A, ϵ 24000, were also found. These bands cannot be considered as *o-benzene-pyridine* spectrum bands, which correspond to 6-methoxy-8-aminoquinoline, as they did not disappear when the hydrogen chloride concentration was increased by factors of 5 and 50. It would be more correct to consider them bands
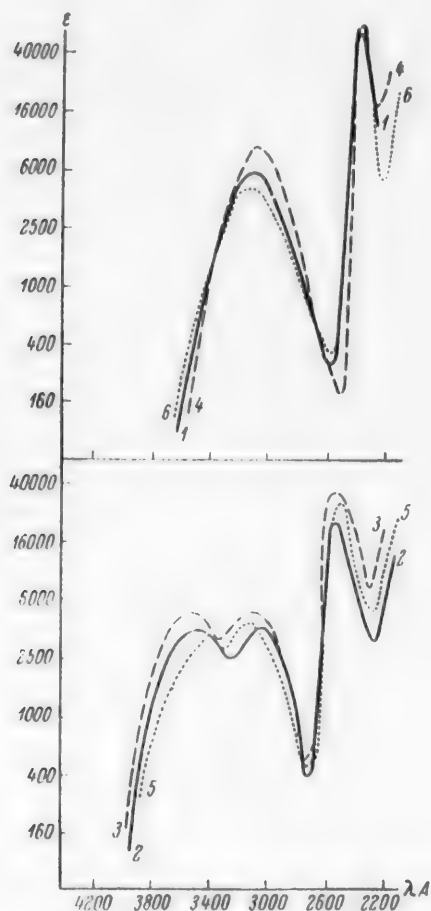
Fig. 3. Absorption spectra. 1) Plasmocide in an ethanolic HCl solution (molar ratio 1 : 20), 2) plasmocide in an ethanolic HCl solution (molar ratio 1 : 100), 3) plasmocide in ethanol, 4) plasmocide in an ethanolic HCl solution (molar ratio 1 : 1000), 5) plasmocide in a 5 M ethanolic HCl solution, 6) 6-methoxy-8-aminoquinoline in an ethanolic HCl solution (molar ratio 1 : 1000), 7) plasmocide in 7 m sulfuric acid.
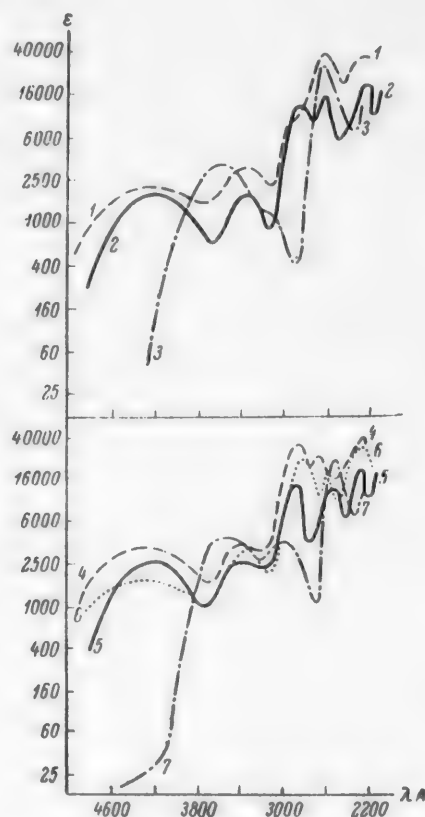
Fig. 4. Absorption spectra. 1) Neoplasmoquin in concentrated sulfuric acid, 2) plasmocide in concentrated sulfuric acid, 3) 6-methoxy-8-aminoquinoline in concentrated sulfuric acid, 4) 8-aminoquinoline in concentrated sulfuric acid, 5) 6-methoxyquinoline in concentrated sulfuric acid, 6) quinoline in concentrated sulfuric acid.

of such ortho-benzene derivatives as o-nitroaniline or o-hydroxybenzaldehyde. This was confirmed by the similarity of the bands on the 2-hydroxybenzaldehyde curve with the corresponding bands on the curves of 6-methoxy-8-aminoquinoline in ethanol solutions of hydrogen chloride (Fig. 2, curves 1 and 2). From this the given bands of the *ortho-type* 6-methoxy-8-aminoquinoline ion are provisionally called *o-nitroaniline* absorption bands.

The similarity of the curves of 6-methoxy-8-aminoquinoline and 8-aminoquinoline in an ethanol solution of HCl with a molar ratio of 1 : 1000 (Fig. 2, curves 5 and 1, 3, Fig. 1, curves 6 and 2, 4) was indicated by the

appearance of "o-aminostyrene" absorption bands in their spectra. The difference due to the methoxy group was the fact that the 8-aminoquinoline ion spectrum had an "o-phenylenediamine" band and no "o-nitroaniline" absorption band while the 6-methoxy-8-aminoquinoline ion, on the contrary, had an "o-nitroaniline" band and no " o-phenylenediamine" absorption band (Fig. 2, curves 1 and 4, Fig. 1, curves 6, 2 and 3).
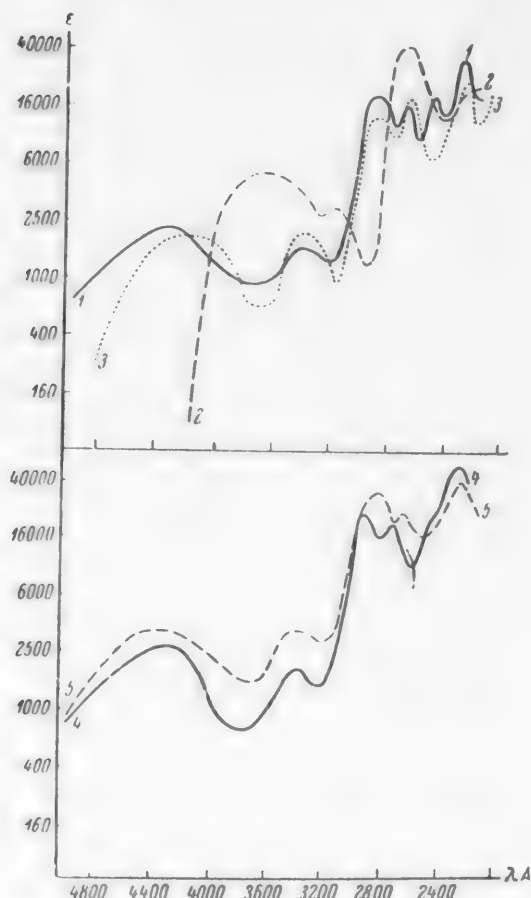
Fig. 5. Absorption spectra. 1) Quinocide in an ethanolic HCl solution (molar ratio 1 : 100), 2- quinocide in ethanol, 3) plasmocide in an ethanolic HCl solution (molar ratio 1 : 100), 4) quinocide in an ethanolic HCl solution (molar ratio 1 : 1000), 5) plasmocide in an ethanolic HCl solution (molar ratio 1 : 1000).
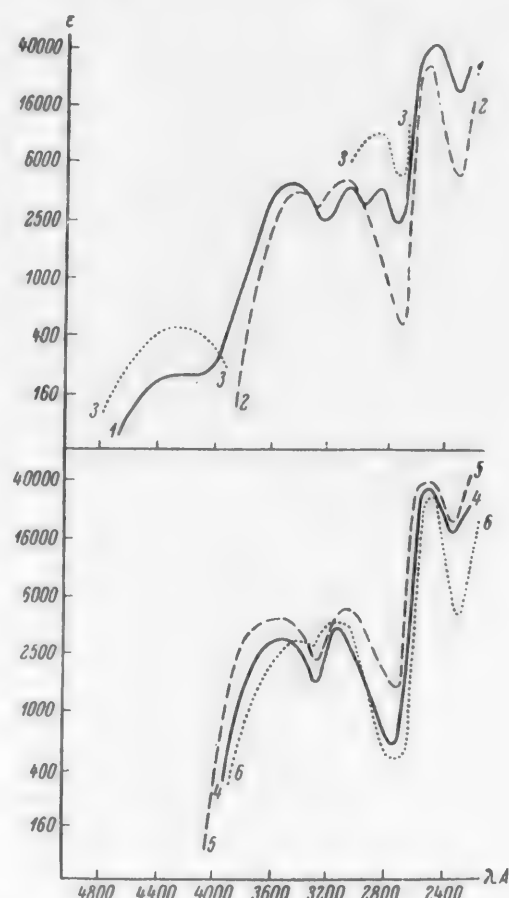
Fig. 6. Absorption spectra. 1) Quinocide in 5 M sulfuric acid, 2) 6-methoxyquinoline in 5 M sulfuric acid, 3) 6-methoxy-8-aminoquinoline in 4 M ethanolic HCl solution (part of curve), 4) quinocide in 10 M sulfuric acid, 5) quinocide in concentrated sulfuric acid, 6) 6-methoxyquinoline in concentrated sulfuric acid.

Salt formation at the amino group of 6-methoxy-8-aminoquinoline started in a 4 M ethanol solution of hydrogen chloride (molar ratio 1 : 2000). At this ratio neither of the "o-nitroaniline" bands were found in the spectrum but three new absorption bands appeared, λ_{max} 3510, 3080 and 2520 A (Fig 2, curves 5 and 6). Similar bands were found in the spectrum of the 6-methoxyquinoline salt at the ring nitrogen [10]. Simultaneously with the appearance of the band of the 6-methoxyquinoline ion, the intensity of the "o-aminostyrene" bands of the singly charged ion of 6-methoxy-8-aminoquinoline (salt at the ring nitrogen) fell sharply. This may indicate the formation of an equilibrium between the singly charged and doubly charged ions of 6-methoxy-8-amino-quinoline (Fig. 2, curves 7 and 8) or 8-aminoquinoline (Fig. 1, curves 7 and 8). The singly charged ion of 6-methoxy-8-aminoquinoline was completely converted into the doubly charged one by the effect of concentrated sulfuric acid and this was confirmed by the coincidence of the spectral curves of 6-methoxy-8-aminoquinoline and 6-methoxyquinoline in concentrated sulfuric acid (Fig. 4, curves 3 and 5) and those of 8-aminoquinoline

and neoplasmoquin with that of quinoline in concentrated sulfuric acid (Fig. 4, curves 1, 4 and 6).

The spectral characteristics of plasmocide in ethanol solutions of hydrogen chloride (Fig. 3, curves 1, 2, and 3) and in sulfuric acid (Fig. 4, curves 2, 3 and 5; cf. Fig. 3, curves 7 and 5) are approximately the same as those of 6-methoxy-8-aminoquinoline examined above. The diethylaminopropyl radical had very little effect on the spectrum of the salt (Fig. 3, curves 4, 5 and 6). The behavior of quinocide in ethanol solutions of hydrogen chloride and in sulfuric acid differed little from that of plasmocide (Fig. 5, curves 1-5; Fig. 6, curves 1, 4, 5 and 2, 3 and 6).

DISCUSSION OF RESULTS

The complex interrelations between the substituents in the 8-aminoquinoline salt at the ring nitrogen are explained quite satisfactorily on the basis of the experimental data given above if this salt is considered as a benzene derivative with one electron-acceptor and two electron-donor substituents in positions 1, 2 and 3. Benzene derivatives with three such substituents were studied spectrographically by N. A. Valyashko [11]. In analogy with the rules he established, the appearance of two "o-aminostyrene" bands in the spectrum of the 8-aminoquinoline salt at the ring nitrogen, may be explained by the formation of a conjugated system (I) similar to that in an unsubstituted quinoline ion (II) [2]. The 8-NHR group does not participate in the conjugation with the ring nitrogen, which is denoted by a dotted line in (I). However, the appearance in the spectrum on neoplasmoquin salt at the ring nitrogen of an "o-phenylenediamine" band with a fine structure, is explained by the 8-NHR group being involved in the reaction with the ring and with the ring nitrogen (III).

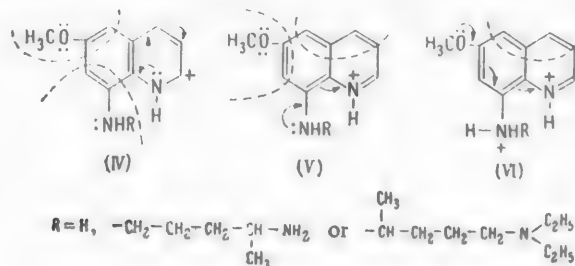$$R = H \quad \text{or} \quad -CH-CH_2-CH_2-CH_2-N\begin{smallmatrix}C_2H_5\\ \\C_2H_5\end{smallmatrix}$$
$$\quad\quad\quad\quad\quad\overset{CH_3}{|}$$
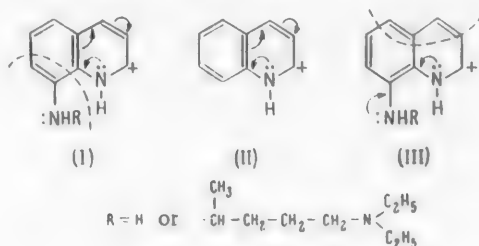
Salt formation at the 8-NHR group of 8-aminoquinoline proceeds with difficulty in comparison, for example, with salt formation at the amino group of 6-aminoquinoline [15] and is accompanied by a return to the quinoline ion spectrum (II). As regards salt formation at the ring nitrogen of 6-methoxy-8-aminoquinoline, its corresponding ion should be considered as a benzene derivative with four substituents. One of these substituents, the vinyl group, is capable of accepting electons, while the other three, including also the ring nitrogen, donate electrons. Then the conditions for the electron transfers are approximately the same as those established for ions of unsubstituted quinoline [2] or 6-methoxyquinoline [10]. Benzene derivatives with the four substituents in positions 1, 2, 3 and 5, mentioned above, have not been studied spectrographically so their spectra cannot be compared with those of the singly charged 6-methoxy-8-aminoquinoline ion. However, conjugation of the vinyl group with the π-electons of the benzene ring and the ring nitrogen (as a substituted amino group) is indicated by the appearance in the spectrum of the 6-methoxy-8-aminoquinoline ion (IV) of two "o-aminostyrene" bands with maxima at about λ equals 4200 and 2830 A. Under these conditions the 8-NHR and 6-OCH$_3$ groups, designated by a dotted line in formula (IV), are not included in the reaction with ring

$$R = H, \quad -CH_2-CH_2-CH_2-\overset{CH_3}{\underset{CH_3}{\overset{|}{\underset{|}{CH}}}}-NH_2 \quad \text{or} \quad -CH-CH_2-CH_2-CH_2-N\begin{smallmatrix}C_2H_5\\ \\C_2H_5\end{smallmatrix}$$

nitrogen but are conjugated separately with the π-electrons of the benzene ring. Their joint action displaces the "o-aminostyrene" bands strongly toward longer wavelengths in comparison with the same bands of the quinolinium ion.

In the same case, when the 8-NHR group of 6-methoxy-8-aminoquinoline is conjugated with a positively charged ring nitrogen through the π-electron system of the benzene ring, then the methoxy and vinyl groups do not participate in the conjugation with the ring nitrogen (designated by dotted lines in formula (VI)). However, they may be conjugated separately with the π-electrons of the benzene ring. Under their joint action the bands, provisionally named "o-nitroaniline" bands and corresponding in (V) to conjugation of the positively charged ring nitrogen with the ring and the amino group, are only slightly displaced toward longer wavelengths. Only when a salt is formed at the 8-NHR group and the ring nitrogen of (VI) may the methoxy group of 6-methoxy-8-aminoquinoline be conjugated with the ring and the ring nitrogen. Then the amino group, forming a salt, is eliminated from the chain of conjugation with the ring nitrogen and this makes it possible for the methoxy group to participate in electron transfers similar to the electron transfers occuring in the 6-methoxyquinolinium ion [1, 10].

Thus, the ring nitrogen in 6-methoxy-8-aminoquinoline ion is capable of participating in electron transfers as an electron-donor and an electron-acceptor, in contrast to the 8-aminoquinoline ion, where the ring nitrogen is only capable of donating electons.

We would like to thank O. Yu. Magidson and V. L Stavrovskaya for the preparations for the spectral investigatiion.

SUMMARY

1. The complex spectrum of the singly charged 8-aminoquinoline ion was interpreted as that of a benzene derivative with one electron-acceptor and two electron-donor substituents in positions 1, 2, and 3 and it was established that in this case the ring nitrogen participates in electron transfers as a substituted amino group, reacting with the vinyl (electron acceptor) or with the 8-NHR (electron-donor) groups through the π-electron system of the benzene ring.

2. The complex spectrum of the singly charged 6-methoxy-8-aminoquinoline ion (salts at the ring nitrogen) was interpreted as that of a benzene derivative with one electron-acceptor and three electron-donor substituents in positions 1, 2, 3, and 5 and it was established that the ring nitrogen is capable of participation in electron transfers either as a substituted amino group, entering conjugation with the vinyl group (electron-acceptor) or as a positively charged nitrogen, entering conjugation with the 8-NHR group through the π-electron system of the benzene ring.

3. It was established that salt formation at the 8-NHR group of 8-aminoquinoline is accompanied by a reversion to the spectrum of a quinolinium ion and to the spectrum of the 6-methoxyquinolinium ion in the case of 6-methoxy-8-aminoquinoline.

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NEW METHOD OF SYNTHESIZING ALKYLNAPHTHALENES

B. N. Dolgov and S. A. Bnatov

The present work is a continuation of our investigations on the synthesis of aromatic hydrocarbons in the presence of aluminum metal.

In previous papers [1-3] we studied the synthesis and reactions of alkylbenzenes in the presence of aluminum chloride, prepared by Radziewanowski's method. In the present investigation, we examined the synthesis of alkylnaphthalenes based on the reaction of naphthalene with some alkyl halides in the presence of metallic aluminum, activated with a small amount of aluminum chloride. Up to now the literature has contained only a small number of papers (4-6), largely devoted to the synthesis of benzene derivatives.

We synthesized alkylnaphthalenes by the following scheme:

$$C_{10}H_8 + RHal \xrightarrow[70-95°]{Al+AlCl_3} C_{10}H_7R + HHal.$$
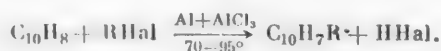
The syntheses required 1-2% of metallic aluminum (of the weight of naphthalene used in the reaction) and 0.03-0.05% of aluminum chloride. Excess aluminum and prolonged heating resulted in the formation of polyalkylnaphthalenes.

The alkylating agents used were ethyl bromide, n-propyl and n-butyl chlorides and isoamyl chloride. During the alkylation of the naphthalene, isomerization of the alkyl radical was observed and as a result the main reaction products were iso- and sec -alkylnaphthalenes. One may assume from this that alkylation in this case proceeded through the stage of unsaturated hydrocarbon formation, for example, by the reactions

$$CH_3CH_2CH_2Cl \xrightarrow{Al+AlCl_3}_{t°} CH_3CH=CH_2 + HCl$$

$$C_{10}H_8 + CH_3CH=CH_2 \xrightarrow{Al+AlCl_3}_{t°} C_{10}H_7CH(CH_3)_2$$
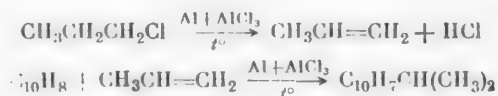
Such an isomerization was first established by Gustavson [7, 8] in the alkylation of benzene and toluene with normal alkyl halides in the presence of aluminum chloride. Similar observations were made by M. L. Konovalov [9, 10] and other authors [11, 12].

A characteristic of the method proposed is the formation of mainly and, in certain cases, wholly β-alkylnaphthalenes, which corresponds to drastic reaction conditions (high temperature and high isomerizing capacity of the catalyst) and agrees with earlier reports on the subject [13, 14]. However, one may suppose that the primary reaction products are α-alkylnaphthalenes [14, 15], which are isomerized under drastic reaction conditions to β-alkylnaphthalenes.

The structures of the alkylnaphthalenes were proved by preparation of their picrates and by their oxidation with 5% HNO_3 at 170-180° in sealed tubes. The properties of the hydrocarbons we isolated are summarized in the table.

EXPERIMENTAL

The starting materials used for the syntheses were commercial naphthalene and pure alkyl halides (ethyl bromide and propyl, butyl and isoamyl chlorides).

Properties of Alkylnaphthalenes

Alkylnaphthalene	Boiling point at atmospheric pressure	Boiling point in vacuum (mm)	n_D^{20}	d_4^{20}	Found (%) C	Found (%) H	Calc. (%) C	Calc. (%) H	Yield (in %) on tot. yield on alkylnaphthalenes	Yield (in %) on theoret. am't monoalkylnaphthalenes
α-Ethylnaphthalene	258.3°	135—136° (18)	1.6060	0.9916	92.19	7.81	92.22	7.78	21	57
β-Ethylnaphthalene	251.0	126—127 (18)	1.5593	1.0021	92.32	7.84	92.22	7.78	52	—
Diethylnaphthalene	—	149—150 (18)	1.6013	0.9932	91.16	8.80	91.25	8.75	27	
β-Isopropylnaphthalene	268.9	118 (12)	1.5864	0.9791	91.73	8.25	91.78	8.22	88	65
Diisopropylnaphthalene	279.3	144 (12)	1.5648	0.9681	90.45	9.54	90.56	9.44	12	
α-sec-Butylnaphthalene	276.6	126—128 (8—10)	1.5687	0.9751	91.20	8.81	91.3	8.7	23	47
β-sec-Butylnaphthalene	282.5	120—121 (8—10)	1.5821	0.9764	91.24	8.75	91.3	8.7	50	
Di-sec-butylnaphthalene	310—313	148—150 (8—10)	1.5600	0.9537	89.91	10.1	89.97	10.03	27	
α-sec.-Isoamylnaphthalene	289	130—131 (5—7)	1.5772	0.9751	90.73	9.25	90.85	9.15	26	
β-sec.-Isoamylnaphthalene	296	136—138 (5—7)	1.5712	0.9698	90.80	9.23	90.85	9.15	64	46
Di-sec.-isoamylnaphthalene	318—320	158—160 (5—7)	—	0.9621	89.41	10.67	89.48	10.52	10	

As a result of a series of preliminary syntheses under various conditions (with various temperatures, amounts of metallic aluminum and aluminum chloride, reaction component ratios and experiment durations) a synthesis procedure was developed which differed slightly from that normally accepted. Into a flask fitted with a reflux condenser, a stirrer and a dropping funnel was placed a weighed amount of naphthalene (usually 0.75 mole), 1-2% of the weight of naphthalene of metallic aluminum and 0.03% of aluminum chloride. Then the flask was heated on a boiling water bath and the mixture stirred continuously while the alkyl halide (25% excess compared with an amount equimolecular with the naphthalene) was added dropwise through the dropping funnel. The reaction then rapidly became more vigorous and proceeded at 60-70°. When all the alkyl halide had been added, the reaction mixture was stirred for a further 1-2 hours. The reaction mixture was broken up with a cold solution of acetone in water in a sufficient amount to destroy the aluminum complexes formed during the reaction. When the solvent had been removed, the reaction product was fractionated in vacuum and then several times at atmospheric pressure over sodium. In the latter fractionation, narrow fractions (1-2°) were separated. The yield of narrow fractions of monoalkylnaphthalenes was 45-65% (the maximum yield was obtained with β-isopropylnaphthalene).

We will give a description of one of the experiments.

Alkylation of naphthalene with propyl chloride. 96 g of naphthalene, 78 g of propyl chloride, 2 g of aluminum turnings and 0.03 g of aluminum chloride were used. After the procedure given above, we isolated the following substances.

1. β-Isopropylnaphthalene 86.7 g (65%):

B. p. 268-269° (760 mm), 118° (12 mm), d_4^{20} 0.9791, n_D^{20} 1.5864.
Found %: C 91.73, 91.70; H 8.24, 8.30.
$C_{13}H_{14}$. Calculated %: C 91.78; H 8.22.

The picrate was prepared by Smith's method [16]. The m. p. was 88-90° (according to literature data [13]: 89-90°).

Oxidation of the fraction with 5% HNO_3 in a sealed tube at 170-180° for 10 hours yielded β-naphthoic acid with m. p. 182°.

2. β,β'-Diisopropylnaphthalene 12.4 g (8%):

B. p. 279-280° (760 mm), 144° (12 mm), d^{20}_4 0.9681, $n^{20}D$ 1.5648.

Found %: C 90.45, 90.60; H 9.54, 9.51. $C_{10}H_{20}$. Calculated %: C 90.56; H 9.44.

Picrate: m. p. 84-86° (according to literature data [13]: m. p. 86°).

3. Fraction 138-145° (1 mm), d^{20}_4 0.9584, $n^{20}D$ 1.5600; a thick yellow oil.

Found %: C 89.0, 89.5; H 10.5, 10.9. $C_{19}H_{26}$. Calculated %: C 89.8; H 10.2

From a comparison of analysis data with literature data [13] (d^{20}_4 0.9591, $n^{20}D$ 1.5605), we assumed that this fraction was triisopropylnaphthalene.

4. Fraction 250-295 (1 mm), a thick orange oil; this was not examined in detail.

When the oils had been distilled off, a coke-like product remained in the flask, which was insoluble in organic solvents and which was not examined further.

SUMMARY

The possibility of preparing alkylnaphthalenes by the reaction of naphthalene with alkyl halides in the presence of metallic aluminum, activated with a small amount of aluminum chloride, was demonstrated. The yield of monoalkylnaphthalenes reached 65%.

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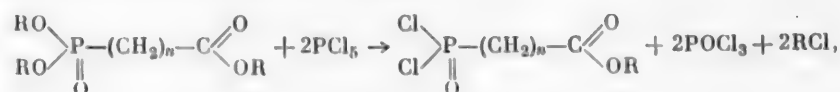[16] S. N. Morrell, G. B. Pickering, and L. C. Smith, J. Inst. Petr. 34, 677 (1948).

*Original Russian pagination. See C.B. Translation.

HALIDES OF ESTERS OF PHOSPHONOCARBOXYLIC ACIDS

II. DICHLORIDES OF C-ALKYL ESTERS OF PHOSPHONOCARBOXYLIC ACIDS

K. A. Petrov, F. L. Maklyaev and M. A. Korshunov

It has been shown previously that P-monochlorides of dialkyl esters of phosphonocarboxylic acids are formed in good yields under mild conditions by the action of phosphorus pentachloride on the neutral esters of phosphonocarboxylic acids. [*] It was shown in the present work that the dichlorides of the C-alkyl esters of these acids are formed by the action of excess phosphorus pentachloride on the neutral esters of phosphonoacetic and β-phosphonopropionic acids under more drastic conditions:

$$\begin{array}{c}RO \\ RO\end{array}\!\!>\!\!P-(CH_2)_n-C\!\!<\!\!\begin{array}{c}O \\ OR\end{array} + 2PCl_5 \rightarrow \begin{array}{c}Cl \\ Cl\end{array}\!\!>\!\!P-(CH_2)_n-C\!\!<\!\!\begin{array}{c}O \\ OR\end{array} + 2POCl_3 + 2RCl,$$

where n = 1 or 2.

The yield of the dichlorides reaches 68-85%. The ester group at the carbon atom is not replaced by chlorine with even a large excess of phosphorus pentachloride and prolonged heating of the reaction mixture to 115-120°; only the two ester groups located at the phosphorus atom are replaced by chlorine.

The possibility of preparation of P-mono- and P,P-di-chlorides of esters of phosphonocarboxylic acids is evidently connected with the different degrees of difficulty of the replacement of two ester groups attached to the phosphorus atom by chlorine, which event occurs with more difficulty in the case of esters of phosphonoacetic acid than that of esters of phosphonopropionic acid.

The dichloride of C-ethyl ester of phosphonoacetic acid, in contrast to the monochlorides of esters of phosphonoformic acid, could not be prepared by chlorination of a solution consisting of phosphorus trichloride and triethyl phosphonoacetate with gaseous chlorine. The chlorination of the methylene group of the phosphonoacetic ester and the formation of the dichloride of the C-ethyl ester of phosphonodichloroacetic acid (yield about 57%) take place during the passage of chlorine into the reaction mixture in this case, along with the replacement of the ester groups, attached to phosphorus, by chlorine atoms.

$$\begin{array}{c}C_2H_5O \\ C_2H_5O\end{array}\!\!>\!\!P-CH_2-C\!\!<\!\!\begin{array}{c}O \\ OC_2H_5\end{array} + 2PCl_3 + 4Cl_2 \rightarrow$$

$$\rightarrow \begin{array}{c}Cl \\ Cl\end{array}\!\!>\!\!P-CCl_2-C\!\!<\!\!\begin{array}{c}O \\ OC_2H_5\end{array} + 2POCl_3 + 2C_2H_5Cl + 2HCl$$
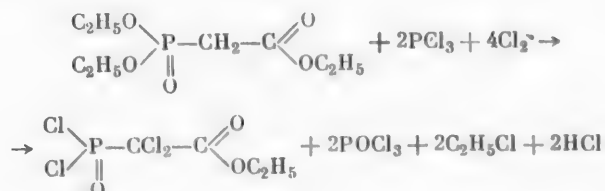
The dichloride of C-ethyl ester of phosphonodichloroacetic acid is a colorless liquid with an irritating ordor; it is soluble in organic solvents. The dichloride is hydrolyzed by water with cleavage of two chlorine

atoms, which can be quantitatively determined by the Volhard method. The total chlorine content is determined after combustion of the substance or by the Stepanov method. The analytical data on carbon, hydrogen, phosphorus and chlorine correspond to the dichloride of the ethyl ester of phosphonodichloroacetic acid. The location of the ester group in this substance is proved rigidly by the reaction of the dichloride with hydrogen fluoride or potassium bifluoride, which yields the ethyl ester of dichloroacetic acid; the latter may be formed under these conditions only as the result of cleavage of the C-ethyl ester of the dichloride of phosphono-dichloroacetic acid at the C-P link:
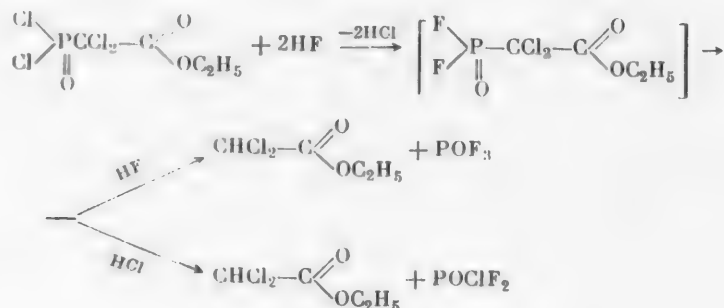
It is possible that the difluoride is formed first and that this undergoes decomposition under the influence of either hydrogen fluoride or the evolving hydrogen chloride.

<div align="center">EXPERIMENTAL</div>

Dichloride of C-ethyl ester of phosphonoacetic acid. 39 g of phosphorus pentachloride was added in portions over one hour to 20 g of triethyl phosphonoacetate with energetic stirring. The mixture was heated on a steam bath for 1.5 hours, cooled, sealed into a glass tube and heated for five hours to 115-120°. Then dry sulfur dioxide was passed into the mixture for twenty minutes at room temperature, during which a noticeable heat evolution occurred. A fraction with b. p. 75-80° (0.05 mm) was isolated by the vacuum distillation of the residue obtained after the distillation of thionyl chloride and phosphorus oxychloride. 4.8 g of a brown tar remained in the flask. 12.55 g (68%) of the substance having the constants shown below was obtained after a redistillation:

b. p. 76-78° (0.05 mm), d^{23}_4 1.5038, $n^{23}D$ 1.4774.
Found %: Cl 34.50, 35.04. $C_4H_7O_3PCl_2$. Calculated %: Cl 34.61.

The dichloride of C-ethyl ester of phosphonoacetic acid is a dense, colorless liquid with a penetrating odor; it fumes slightly in air, is dissoved by organic solvents and is hydrolyzed by water. It decomposes above 135-140° with formation of a brown tar which dissolves in water yielding a cherry-red color.

Dichloride of C-ethyl esters of phosphonopropionic acid. 79.5 g of phosphorus pentachloride was added in small portions with stirring to 43 g of triethyl phosphonopropionate. The reaction proceeded energetically, with heat evolution. The mixture was heated for 30 minutes at 65° and one hour in a sealed tube at 120°. Dry sulfur dioxide was passed into the mixture for 20 minutes at room temperature, after cooling. The residue after the removal of thionyl chloride and phosphorus oxychloride was distilled under vacuum. 33.7 g (85.5%) of the substance with the following constants was isolated:

b. p. 89-91° (0.03-0.05 mm), d^{20}_4 1.5602, $n^{20}D$ 1.4640.
Found %: C 27.12, 27.24; H 4.17, 4.16; P 13.96, 13.79; Cl 32.18, 32.42. $C_5H_9O_3PCl_2$. Calculated %: C 27.45; H 4.14; P 14.15; Cl 32.38.

The dichloride is a mobile, colorless liquid with a penetrating odor; it is soluble in organic solvents and is hydrolyzed by water. It turns yellow green in color after storage.

Dichloride of C-ethyl ester of phosphonodichloroacetic acid. Dry chlorine was passed into a mixture of 100 g of triethyl phosphonoacetate and 184 g of phosphorus trichloride, with stirring and ice water cooling, at such a rate that the temperature within the flask failed to rise over 60°. The considerable heat evolution

occurred only in the beginning of the passage of chlorine. The introduction of chlorine was stopped after the formation of a considerable amount of phosphorus pentachloride precipitate and the mixture was then heated on a water bath to 70-75° until the precipitate disappeared. The chlorine passage and the heating were performed periodically and were continued until the formation of the precipitate failed to occur any longer (about 9 hours). Then the mixture was cooled with ice-salt, the resulting phosphorus pentachloride precipitate (36.5 g) was filtered off and dry sulfur dioxide was introduced for 30 minutes into the filtrate for the decomposition of the dissolved phosphorus pentachloride. The residue after the distillation of thionyl chloride and phosphorus oxychloride under a slight vacuum was fractionated. The following fractions were collected: 1st 75-116° (8 mm), 18.1 g; 2nd 116-122° (8 mm), 74.5 g; residue 12 g.

The first fraction was not examined. 70.2 g (57.6%) of the dichloride with b. p. 120-122° (8 mm), d_4^{20} 1.5603, n_D^{20} 1.4920, was isolated by redistillation of the second fraction.

Found %: C 17.50, 17.55; H 2.18, 2.31; P 11.11, 10.88; Cl (total) 51.62, 51.60; Cl (acid chloride)* 26.03; 26.13. $C_4H_5O_3PCl_4$. Calculated %: C 17.53; H 1.83; P 11.31; Cl (total) 51.76; Cl (acid chloride)* 25.88.

The dichloride is a mobile, colorless liquid with an irritating odor; it is readily soluble in organic solvents and is hydrolyzed by water; it reacts energetically with ammonia and amines and does not react with hydrogen chloride.

Cleavage of dichloride of C-ethyl ester of phosphonodichloroacetic acid. a) Cleavage by hydrogen fluoride. The reaction was run in a copper Wurtz flask connected to a Tishchenko absorption flask with sulfuric acid 11.7 g of the dichloride was added slowly dropwise with ice-salt cooling to 7.1 g of anhydrous hydrogen fluoride, after which the mixture was left for 50 minutes at room temperature; evolution of gaseous products was observed but these were not examined. Then the mixture was heated for 50 minutes at 50°. 20 ml of absolute ether and 10 g of calcined potassium fluoride was added to the reaction mixture, cooled with ice-salt, for the removal of excess hydrogen fluoride. The ethereal solution was filtered after a brief standing period and the precipitate was washed with ether. The ether was distilled from the filtrate and the residue was vacuum distilled. Two fractions were collected: 1st 63-69° (37 mm), 0.45 g, and 2nd 69-71° (37 mm), 2.3 g.

The second fraction was washed twice with water, dried with anhydrous magnesium sulfate and distilled; b. p. 153-154° (745 mm), n_D^{20} 1.4380. The substance did not contain phosphorus or fluorine; chlorine was detected only after a fusion with sodium. The substance was the ethyl ester of dichloroacetic acid.

Found %: Cl 45.0, 45.1. $C_4H_6O_2Cl_2$. Calculated %: Cl 45.22.
From the literature data: b. p. 158°, n_D^{20} 1.4380.

b) Cleavage with potassium bifluoride. 5 g of the dichloride was slowly added with stirring and water cooling to 4 g of finely powdered potassium bifluoride; a heating-up of the reaction mixture was observed. Then the mixture was heated for 1.5 hours at 100° and for two hours at 140°. The precipitate was filtered off after cooling and was thoroughly washed with ether; the filtrate was distilled under vacuum after the ether had been distilled from it. The following fractions were collected: 1st 62-69° (37 mm), 0.2 g, and 2nd 69-71° (37 mm), 2.3 g.

The second fraction had b. p. 153-154° (743 mm), and n_D^{20} 1.4380 after a redistillation; it did not contain phosphorus or fluorine and was the ethyl ester of dichloroacetic acid.

SUMMARY

1. The action of excess phosphorus pentachloride on triethyl esters of phosphonoacetic and phosphonopropionic acids with heating leads to the formation of dichlorides of C-ethyl esters of these acids.

2. The dichloride of C-ethyl ester of phosphonodichloroacetic acid is obtained by chlorination of a mixture of phosphonoacetic ester and phosphorus trichloride; this product is cleaved at the phosphorus—carbon bond by hydrogen fluoride or potassium bifluoride.

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*Acid chloride, i.e., phosphorus-bound chlorine was determined in samples of the substance which had been hydrolyzed with dilute alkali solutions at room temperature. Under these conditions the chlorine atoms bound to carbon are not hydrolyzed.
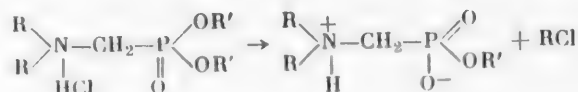
SYNTHESIS OF ACID ESTERS OF DIALKYLAMINOALKYLPHOS-
PHONIC ACIDS

K. A. Petrov, F. L. Maklyaev and N. K. Bliznyuk

Aminophosphonic acids exist in the form of inner salts like the aminocarboxylic acids. Thus, the ethyl ester of aminomethylphosphonic acid, prepared by alkylation of ammonia with the diethyl ester of chloromethylphosphonic acid [1, 2], is an inner salt which produces a neutral reaction in aqueous solutions. The acid inner salt of aminomethylphosphonic acid, prepared by hydrolysis of N-acylaminomethylphosphonic dichloride [3,4] and N-phthalimidomethylphosphonate ester [5], is also known.
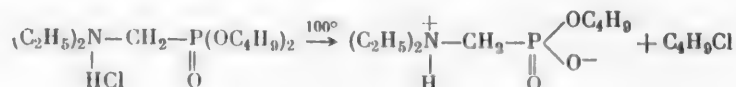
Ethylenediaminotetramethylenephosphonic acid and others belong among similar substances. The latter substances, which resemble the ethylenediaminotetracetic acid, have been recommended as effective complex-formers [6].

Some aminomethylphosphonate hydrochlorides have been prepared in this work and a simple method of their conversion into the inner salts was discovered. This method is based on the thermal decomposition of the hydrochlorides of neutral esters of dialkylaminoalkylphosphonic acids. The dialkylaminomethylphosphonate hydrochlorides, in contrast to the amine hydrochlorides, do not cleave alkyl halides or alkenes by dealkylation of the amino group during thermal decomposition, but are transformed into the inner salts of esters of dialkyl-aminoalkylphosphonates, by evolving an alkyl halide formed from the chlorine ion and the radicals of the ester groups.

$$\begin{matrix} R \\ R \end{matrix}\!\!N\!-\!CH_2\!-\!P\!\!\begin{matrix} OR' \\ \\ O \end{matrix} \rightarrow \begin{matrix} R \\ R \end{matrix}\!\!\overset{+}{N}\!-\!CH_2\!-\!P\!\!\begin{matrix} O \\ \\ O^- \end{matrix}OR' + RCl$$
$$\qquad\quad |$$
$$\qquad HCl \qquad\qquad\qquad H$$

Thus, for example, ethyl chloride is evolved during the decomposition of the diethyl diethylaminomethyl-phosphonate in quantitative amounts and the monoethyl ester of diethylaminomethylphosphonic acid is formed; this is a crystalline substance, readily soluble in water, alcohol, hot acetone, difficultly soluble in benzene, practically insoluble in ether.

The order of cleavage of the alkyl groups was shown by the example of a thermal decomposition of hydro-chlorides of neutral esters of dialkylaminomethylphosphonic acid with various radicals at the atoms of phosphor-us and nitrogen. Thus, butyl chloride and the monobutyl ester of diethylaminomethylphosphonic acid were iso-lated in quantitative yields during the heating of the hydrochloride of the dibutyl ester of diethylaminomethyl-phosphonic acid, the latter product being a viscous sirupy mass which was readily soluble in water.

$$(C_2H_5)_2N\!-\!CH_2\!-\!P(OC_4H_9)_2 \overset{100°}{\longrightarrow} (C_2H_5)_2\overset{+}{N}\!-\!CH_2\!-\!P\!\!\begin{matrix} OC_4H_9 \\ \\ O^- \end{matrix} + C_4H_9Cl$$
$$\quad |\qquad\qquad\;\| \qquad\qquad\qquad\qquad |\qquad\quad\|$$
$$\quad HCl\qquad\;\; O \qquad\qquad\qquad\qquad H\qquad O$$

Similar results were also obtained in the thermal decomposition of the hydrochloride of the diethyl ester of dimethylaminomethylphosphonic acid. Ethyl chloride and the monoethyl ester of dimethylaminomethylphos-phonic acid are formed on heating this hydrochloride, the latter product having the form of colorless deliques-cent crystals, which are readily soluble in water, chloroform and alcohol, sparingly soluble in benzene and chlorobenzene as well as hot acetone, and insoluble in ether.

$$(CH_3)_2{-}N{-}CH_2{-}P(OC_2H_5)_2 \xrightarrow{100^\circ} (CH_3)_2\overset{+}{N}{-}CH_2{-}P{\Big\langle}\begin{smallmatrix}OC_2H_5\\[2pt]O^-\end{smallmatrix} + C_2H_5Cl$$
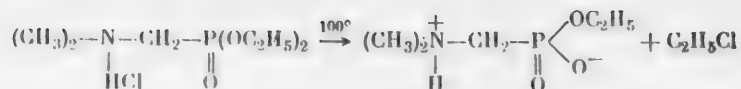
The aqueous solutions of the monoesters have a neutral reaction which fact indicates the characteristic pecularity of the structure.

The hydrofluorides of the neutral esters of dialkylaminomethylphosphonic acid are thermally stable substances in contrast to the hydrochlorides. Thus, for example, heating of the hydrofluoride of the diethyl ester of dimethylaminomethylphosphonic acid for three hours at 135° failed to lead to any changes.

The hydrochlorides and the hydrofluorides of esters of dialkylaminomethylphosphonic acid were prepared by the action of the gaseous hydrogen halides on the esters dissolved in organic solvents. The hydrochlorides of the esters of dialkylaminomethylphosphonic acids are transformed into the free bases on being treated with triethylamine.

EXPERIMENTAL

The hydrochloride of the diethyl ester of dimethylaminomethyl phosphonic acid and its reaction with triethylamine. Hydrogen chloride was passed into a solution of 20.1 g of diethyl dimethylaminomethylphosphonate in 100 ml of dry ether with cooling to −15° and stirring until the heat evolution ceased, the rate of reaction being so adjusted as to prevent a temperature rise above −5°. The colorless crystalline precipitate was filtered off and washed several times with ether. 23 g (97.4%) of the product was obtained after ization; m. p. 95°.

Found %: Cl 15.2, 15.4. $C_7H_{19}O_3NClP$. Calculated %: Cl 15.35.

This formed hygroscopic colorless crystals which were readily soluble in water, chloroform, alcohol and hot acetone and insoluble in benzene and ether.

11.8 g of the hydrochloride and 100 ml of dry ether was placed into a three-necked flask with a stirrer, a thermometer, a dropping funnel and a reflux condenser, and 7.5 g of triethylamine was slowly added with cooling; heat evolution was observed. The mixture was heated for one hour at 35-40°. 6.5 g of triethylamine hydrochloride was isolated, m. p. 254°. 4.1 g of diethyl dimethylaminomethylphosphonate with b. p. 95° (8 mm) was isolated from the filtrate. Literature data: b. p. 88° (3 mm).

The hydrochloride of the dibutyl ester of diethylaminomethylphosphonic acid. Hydrogen chloride was passed into the solution of 20 g of dibutyl diethylaminomethylphosphonate in 100 ml of dry ether as described above. The separation of crystals was not observed. After the solvent had been distilled off, the excess hydrogen chloride was removed under vacuum with the aid of dry benzene which was added periodically to the reaction mixture commensurate with its distillation. 21.5 g (95.5%) of a sirupy distillable and uncrystallizable substance was isolated, which was soluble in water, chloroform and acetone, and insoluble in ether and benzene.

Found %: Cl 11.43, 11.30. $C_{13}H_{31}O_3NClP$. Calculated %: Cl 11.25.

The hydrofluoride of the diethyl ester of dimethylaminomethylphosphonic acid. Hydrogen fluoride was passed into the solution of 5 g of diethyl dimethylaminomethylphosphonate in 20 ml of dry benzene with ice-salt cooling, the gas being introduced slowly until the weight gain of 0.6 g was reached. The solvent and the excess hydrogen fluoride were removed under vacuum. The hydrofluoride was isolated in the form of a viscous glassy mass.

Found %: F 9.4, 9.25. $C_7H_{19}O_3NFP$. Calculated %: F 8.84.

4.5 g of the hydrofluoride was heated for three hours at 120-130° in the Wurtz flask connected to a trap cooled to −70°; no decomposition symptoms were observed.

The monoethyl ester of diethylaminomethylphosphonic acid. 32 g of the hydrochloride of diethyl diethylaminomethylphosphonate was placed in a Wurtz flask connected to a trap chilled to −40° to −70°, and the substance was heated for twenty hours on a steam bath. The reaction mixture crystallized after 7.5 g (98%) of ethyl chloride had evolved. 18.5 g (77.8%) of colorless needle-shaped crystals were isolated after two recrystallizations from dry acetone; m. p. 153°.

Found %: N 7.39, 7.19; H 9.25, 9.27; C 43.09, 43.09. $C_7H_{18}O_3NP$. Calculated %: N 7.18; H 9.23; C 43.08.

The monobutyl ester of diethylaminomethylphosphonic acid. 20 g of the hydrochloride of dibutyl diethyl-aminomethylphosphonate was heated for 28 hours on a steam bath and for 22 hours at 130-140°. 5.6 g of butyl chloride (97%) was evolved. A sirupy mass remained as the residue (12.5 g), this being readily soluble in water (with neutral reaction) alcohol and acetone, and insoluble in ether.

Found %: P 13.77, 13.90. $C_9H_{22}O_3NP$. Calculated %: 13.98.

The monoethyl ester of dimethylaminomethylphosphonic acid. 1.55 g (97%) of ethyl chloride and 4.0 g (97%) of a crystalline substance with m.p. 116° (from acetone), which did not contain chlorine and gave a neutral reaction in aqueous solutions, were isolated from 6 g of diethyl dimethylaminomethylphosphonate hydrochloride after a 20 hour heating on a steam bath.

Found %: P 18.56, 18.61. $C_5H_{14}O_3NP$. Calculated %: P 18.64.

SUMMARY

1. The hydrochlorides and the hydrofluorides of some dialkyl esters of dialkylaminomethylphosphonic acids were prepared and some of their properties were studied.

2. A method of preparation of monoalkyl esters of dialkylaminomethylphosphonic acid was developed through the thermal decomposition of the corresponding hydrochlorides.

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SYNTHESIS OF AMINODIPHOSPHONATES AND AMINOTRI-PHOSPHONATES

K. A. Petrov, F. L. Maklyaev and N. K. Bliznyuk

The aminophosphonates, phosphorus analogs of aminocarboxylic acids, are relatively well known substances. The first representative of this type of substance — aminomethylphosphonic acid — was first prepared in 1943 by the reaction of methylolamides of organic acids with phosphorus trichloride [1]. Later this substance was prepared by alkylation of sodium dibutyl phosphite with bromomethylphthalimide with a subsequent hydrolysis of the phthalimido derivatives [2].
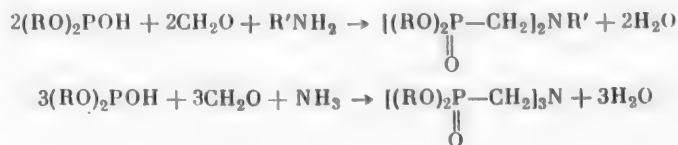
Esters of aminomethylphosphonic acid were prepared by alkylation of ammonia by esters of chloromethylphosphonic acid [3]. The last method of synthesis is a general one, permitting one to prepare any amino- and alkylaminoalkylphosphonates. M. I. Kabachnik showed that α-aminomethylphosphonates are prepared by the reaction of dialkyl hydrogen phosphites with ammonia (amines) and aldehydes (ketones) [4].

Somewhat later Fields prepared by the same method a large number of various aminomethylphosphonates and suggested some other methods of synthesis of these compounds [5].

At this time α-aminoalkylphosphonic acids are readily available substances thanks to the work described above. Aminodiphosphonates, which quite possibly may have some points of practical interest, remain undescribed to this day.

There is an indication in Field's work that in the reaction of aldehydes and phosphites with primary amines there is formed, along with the amino-monophosphonates, a considerable amount of an undistillable oil which was not studied by that author and was considered by him to be an aminodiphosphonate.

The synthesis of aminodiphosphonates and aminotriphosphonates was accomplished in the present investigation in a manner similar to that of the preparation of aminomonophosphonates by the reaction of dialkyl hydrogen phosphites with ammonia (primary amines) and formaldehyde:

$$2(RO)_2POH + 2CH_2O + R'NH_2 \rightarrow [(RO)_2\underset{\underset{O}{\|}}{P}-CH_2]_2NR' + 2H_2O$$

$$3(RO)_2POH + 3CH_2O + NH_3 \rightarrow [(RO)_2\underset{\underset{O}{\|}}{P}-CH_2]_3N + 3H_2O$$

We altered the reagent proportions and the conditions of running the process. Thus, for example, treatment of a mixture of dibutyl hydrogen phosphite and methylamine, taken in 2:1 molar ratio, with the calculated amount of 35-40% formaldehyde solution resulted in bis-(dibutylphosphono)-trimethylamine in yields up to 75%. Bis-(dialkylphosphono)-dimethyl- and tris-(dialkylphosphono)-trimethylamine are formed by the action of formaldehyde on a mixture of the phosphite with aqueous ammonia solution. During the running of the reaction in an aqueous solution, hydrolysis of certain amount of the original phosphite occurs as does that of the resulting aminophosphonate, yielding substances of acidic character; these substances lower the yield of the final products and greatly hinder their isolation. A decomposition of aminodi- and aminotriphosphonates occurs during an attempt to distill the reaction mixture, without a preliminary purification, even at high vacuum, owing to which decomposition the substances could not be isolated. In order to remove the substances with

acidic character, it is necessary to neutralize the mixture, after the completion of the reaction, with alkali, and to extract the resulting aminophosphonates with an organic solvent. The substances, in this case, distill as a rule without decomposition; in some cases it is rational to run the distillation from a small amount of anhydrous potassium or sodium carbonate. The pure aminophosphonates distill without decomposition and are thermally stable substances.

The aminopolyphosphonates, like the diphosphonates, are stable to hydrolysis. They are hydrolyzed to the free acids only after being heated for several hours in concentrated hydrochloric acid in a sealed tube at 130-150°. The free aminodi- and triphosphonic acids exist in the form of inner salts of the following type:

$$
\begin{array}{cc}
\text{HO}\!\!\diagdown & \quad \text{HO}\!\!\diagdown \\
\quad \text{P—CH}_2—\overset{+}{\text{N}}\text{R—CH}_2—\text{P} & \qquad [(\text{HO})_2\text{P—CH}_2]_2\overset{+}{\text{N}}—\text{P}\diagup^{\text{OH}}_{\text{O}^-}
\end{array}
$$
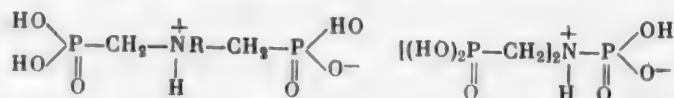
and titrate as tribasic or pentabasic acids, respectively. The properties of the substances prepared by us are given in the table.

Formula	B. p. (pressure in mm)	d_4^{20}	n_D^{20}	MR	
				calc.	found
$[(\text{C}_2\text{H}_5\text{O})_2\text{P—CH}_2]_2\text{NCH}_3$ (P=O)	149—150° (0.5)	1.1340	1.4470	78.67	78.17
$[(\text{iso-C}_3\text{H}_7\text{O})_2\text{P—CH}_2]_2\text{NCH}_3$ (P=O)	146 (0.3)	1.0553	1.4376	97.14	96.33
$[(\text{n-C}_4\text{H}_9\text{O})_2\text{P—CH}_2]_2\text{NCH}_3$ (P=O)	195—197 (1)	1.0320	1.4480	115.61	115.10
$[(\text{C}_2\text{H}_5\text{O})_2\text{P—CH}_2]_2\text{NH}$ (P=O)	150—151 (0.3)	1.1429	1.4470	73.71	74.17
$[(\text{n-C}_4\text{H}_9\text{O})_2\text{P—CH}_2]_2\text{NH}$ (P=O)	195—196 (0.6)	1.0359	1.4490	110.66	111.20
$[(\text{C}_2\text{H}_5\text{O})_2\text{P—CH}_2]_3\text{N}$ (P=O)	202—204 (0.8)	1.1759	1.4534	108.01	107.75
$(\text{HO})_2\text{PCH}_2—\overset{+}{\text{N}}\text{H—CH}_2—\text{P}\diagup^{\text{OH}}_{\text{O}^-}$	Glassy mass				
$[(\text{HO})_2\text{P—CH}_2]_2\overset{+}{\text{N}}—\text{CH}_2—\text{P}\diagup^{\text{OH}}_{\text{O}^-}$	Glassy mass				

Neutral esters of aminopolyphosphonic acids, like the diphosphonates [6], deserve some tests as thermostable lubricating oils, oil additives, plasticizers and hydraulic fluids. The free aminopolyphosphonic acids and their salts, as well as their acid esters and ester salts, which may be readily prepared by partial hydrolysis of the neutral esters, should be rationally tested, like substances of type [7], as complex-formers which yield chelated compounds with metal ions.

EXPERIMENTAL

Bis-(diethylphosphono)-trimethylamine. 22 g of 40% formaldehyde solution was added dropwise with stirring and cooling to a mixture of 40 g of diethyl hydrogen phosphite and 4.5 g of methylamine, cooled to −15°, at such a rate that the temperature failed to rise over 20°. For completion of the reaction, the mixture was slowly (over 30 minutes) heated to 100° and kept for 15 minutes at that temperature. A 5-10% alkali solution was slowly added after cooling until a basic reaction was attained. The product was extracted with benzene, the benzene extracts were washed with water and dried over anhydrous potassium carbonate. 29 g (60%) of the product was obtained; b. p. 149-150° (0.5 mm).

Found %: P 18.56, 18.58; N 4.34. $C_{11}H_{27}O_6NP_2$. Calculated:%: P 18.70; N 4.23.

Bis-(diisopropylphosphono)-trimethylamine. 53 g (54%) of the product was obtained from 88 g of di-iso-propyl hydrogen phosphite, 7.8 g of methylamine and 37.5 g of 40% aqueous solution of formaldehyde, as described above; b. p. 146° (0.3 mm).

Found %: P 16.25; N 3.84, 3.85. $C_{15}H_{35}O_6NP_2$. Calculated %: P 16.00; N 3.62.

Bis-(dibutylphosphono)-trimethylamine. Under similar conditions, 110.4 g (74.6%) of product was obtained from 130.1 g of dibutyl hydrogen phosphite, 10.4 g of methylamine and 50.3 g of 40% Formalin; b. p. 195-197° (1 mm).

Found %: P 14.22, 14.31. $C_{19}H_{43}O_6NP_2$. Calculated %: P 14.00.

Reaction of diethyl hydrogen phosphite with ammonia and formaldehydes. 32.6 g of 40% Formalin was added to the mixture of 60 g of diethyl hydrogen phosphite and 19.9 g of 18.6% aqueous ammonia solution, cooled at −10°, with stirring and at such a rate that the temperature was maintained at about 15-20°. Then the mixture was slowly (over one hour) heated to 100° and kept at that temperature for one hour. The reaction product was fractionated in vacuum, after neutralization with alkali, extraction and drying with potassium carbonate. 10.7 g (15.5%) of bis-(diethylphosphono)-dimethylamine with b.p. 150-151° (0.3 mm) was isolated.

Found %: P 19.32, 19.41. $C_{10}H_{25}O_6NP_2$. Calculated %: P 19.52.

13 g (19.1%) of tris-(diethylphosphono)-trimethylamine with b.p. 202-204° (0.8 mm) was also isolated.

Found %: P 20.02; C 38.34; H 7.62. $C_{15}H_{36}O_9NP_3$. Calculated %: P 19.88; C 38.54; H 7.76.

A large excess of the phosphite and the aldehyde, as well as a more drastic temperature regime led to some increase in the yield of the aminotriphosphonate with a corresponding decrease of the diphosphonate yield.

Reaction of dibutyl hydrogen phosphite with ammonia and formaldehyde. 13.2 g (21.7%) of bis-(dibutyl-phosphono)-dimethylamine with b.p. 195-196° (0.6 mm) was obtained under the conditions of the preceding experiment from 50 g of dibutyl hydrogen phosphite, 14.1 g of 18.6% aqueous ammonia solution and 23.2 g of 40% formaldehyde (the molar ratios of the reactants were 2:1:2, respectively).

Found %: P 14.40, 14.32. $C_{18}H_{41}O_6NP_2$. Calculated %: P 14.42

5.5 g of a substance with b.p. 240-245° (0.8 mm) was also isolated, this being evidently the tris-(dibutyl-phosphono)-trimethylamine.

Hydrolysis of aminodi- and triphosphonates. A mixture of 6 g of bis-(diethylphosphono)-dimethylamine and 20 ml of hydrochloric acid (1:1) was heated in a sealed tube for five hours at 130-140°, after which it was transferred to a flask and was kept under vacuum in a steam bath. Water was gradually added to the mixture as the distillation proceeded, until the chloride ion disappeared from the residue. The residual glassy mass was the aminodi-(methylphosphonic) acid; it titrates with base as a tribasic acid.

Found: equiv.wt. 69.1. Calculated: equiv. wt. 58.4.

Silver salt — colorless crystals which decompose on heating.

Found %: Ag 67.58, 67.42. $C_2H_5O_6NP_2Ag_4$. Calculated %: Ag 68.22.

1.7 g of aminotri-(methylphosphonic) acid was obtained from 3 g of tris-(diethylphosphono)-trimethyl-amine, as described above; this titrates as a pentabasic acid with alkali.

Found: equiv.wt. 60.1. Calculated: equiv.wt. 59.8.

Silver salt — colorless crystals which rapidly darken in light; it decomposes on being heated.

Found %: Ag 69.03. $C_3H_6O_9NP_3Ag_5$. Calculated %: Ag 68.84.

Both acids are glassy masses, soluble in water and insoluble in organic solvents.

SUMMARY

Esters of aminodi- and tri-(methylphosphonic) acids were prepared by the reaction of dialkyl hydrogen phosphites with formaldehyde and primary amines or ammonia. The free acids were prepared by hydrolysis of the esters.

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SULFONIC ACIDS AS BY-PRODUCTS IN THE SULFONATION PROCESSES

V. CONCERNING SOME FACTORS WHICH INFLUENCE THE FORMATION OF SULFONIC ACIDS OF SULFONES

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Up to 25% of diphenylsulfone-3,3'-disulfonic acid (DPS) is formed as the by-product during the sulfonation of benzene with high concentration oleum (60-65% SO_3) to yield the m-disulfonic acid [1]. Similar processes, but in other degrees, occur during the sulfonation of toluene, chlorobenzene [2] and, evidently, many other aromatic compounds with oleum. The formation of sulfone sulfonic acids lowers the yield of the main sulfonic acids and causes complications in the subsequent transformations of these into the hydroxy derivatives [3], into nitro and amino sulfonic acids and other compounds. It appeared interesting in this connection to study the factors which exert their influence on the degree of formation of sulfone sulfonic acids and to establish the sulfonation conditions which lead to a minimum formation of these substances.

We studied the effect of a number of factors on the process of formation of sulfone sulfonic acids with the example of sulfonation of benzene. An examination of the possible reactions, leading to the formation of diphenylsulfone sulfonic acids during the sulfonation of benzene, shows that these may be divided into two groups. The first group includes the reactions leading to the formation of sulfone sulfonic acids through the intermediate origination of diphenylsulfone with its sulfonation being subsequent. The second group includes the reactions in which the sulfone sulfonic acids arise directly from benzenesulfonic acids.

The reactions of the first type may occur only during the sulfonation of the free hydrocarbon; such a stepwise formation of diphenylsulfonesulfonic acid through diphenylsulfone is excluded during the sulfonation of benzenemonosulfonic acid, for example.

It was established by us in this study that diphenylsulfonesulfonic acids are formed by both the first and the second types of reactions. Thus, for example, if one sulfonates benzene with oleum for a time interval that is insufficient for a complete sulfonation, then during the quenching of the sulfonation mixture in water there is isolated a considerable amount of diphenylsulfone, which passes into diphenylsulfonesulfonic acid on further sulfonation [4]. Diphenylsulfonesulfonic acids are formed directly during the sulfonation of the pure benzenemonosulfonic acid with oleum. However, the amount of sulfone sulfonic acids formed in reactions of this type, is somewhat smaller. For example, if up to 25% of DPS is formed during the sulfonation of benzene with 65% oleum [1], only 15% is formed during the sulfonation of benzenemonosulfonic acid under the same conditions (see experiment 3). It is interesting that m-benzenedisulfonic acid practically does not yield any diphenylsulfonesulfonic acids on being treated with oleum (see Experiment 5), under the same conditions.

It was also shown in the process of the study that the concentration of the sulfonating agent (SO_3) at the instant of union with the free hydrocarbon exerts a very great influence on the degree of formation of sulfone sulfonic acids in sulfonation of benzene. The higher is the concentration of the sulfonating agent, the greater amount of diphenylsulfonesulfonic acid is formed in the sulfonation mixture (Table 2). The concentration of the sulfonating agent exerts its influence on the degree of formation of sulfones also during the sulfonation of benzenemonosulfonic acid.

These data show that the greatest amount of sulfone sulfonic acids is formed in the direct reaction of benzene with oleum which contains a considerable amount of SO_3. Starting from this, we ran some comparative experiments on sulfonation of benzene with alteration of the conditions in the first stage — formation of benzenemonosulfonic acid. We studied the known methods of sulfonation of benzene with 100% sulfuric acid, with weak oleum and with high concentration oleum. The stage of the formation of the disulfonic acid was the same in all cases (sulfonation with 65% oleum with a subsequent hold for three hours at 90°). As should have been expected, the best results were obtained in the experiment in which the sulfonation to the monosulfonic acid was run with 100% sulfuric acid (Table 1).

As it was shown by us, the important factor which sharply lowers the rate of the process of formation of diphenylsulfonesulfonic acids during sulfonation of benzene, is the presence of sodium sulfate which is added to oleum in insignificant amounts [5].

TABLE 1

Sulfornation of Benzene with Alteration of Concentration of the Sulfonating Agent During the First State of Sulfonation

| No.of expt. | Content (in %) of | |
	SO_3 in oleum charged for the first stage of sulfonation	diphenysulfone-3,3'-disulfonic acid in the sulfonation mixture, calculated on benzene
14	100% sulfuric acid	1.7
15	20	14.3
6	64.5	24.2

The effect of sodium sulfate on the sulfonation process was established a long time ago and this addition has found a practical application in some processes [6]. However, the explanation of the character of this effect on the sulfonation process has been different for different authors. The most widely distributed, but incorrect, opinion is that sodium sulfate accelerates the sulfonation reaction and allows one to attain a greater depth of the process at considerably lower temperatures, than possible without the addition of sodium sulfate [7]. It was noted in later work that, on the contrary, sodium sulfate has a retarding action in the sulfonation process [8]. We came to the same conclusion, having found a considerable retarding effect of sodium sulfate in the process of sulfonation of benzene to the m-disulfonic acid. Benzene is sulfonated completely by 65% oleum, yielding the disulfonic acid (that of benzene and that of diphenylsulfone) in three hours at 90°, while in the presence of sodium sulfate this occurs in three hours only at 100°, while a direct dependence is observed between the retardation of the reaction rate and the amount of added sodium sulfate. It was noted that the sodium sulfate present in the sulfonation mixture enters into an interaction with sulfuric acid or oleum, that is more deep-seated than a simple solution, since a very great amount of heat is evolved during the addition of sodium sulfate to oleum.

An important consequence of the retardation of the sulfonation reaction after the addition of sodium sulfate is the still greater retardation of the rate of the side reaction of sulfone formation, as the result of which the amount of diphenylsulfonesulfonic acids in the sulfonation mixture is greatly reduced after the addition of sodium sulfate.

The presence of 0.5 mole of sodium sulfate per mole of the benzene that is being sulfonated lowers the content of diphenylsulfonedisulfonic acid in the sulfonation mixture to 1.7%, calculated on benzene, against 24.3% in sulfonation of benzene under similar conditions but without the addition of sodium sulfate (Table 3).

EXPERIMENTAL

Pure reagents were used in the experiments. Oleum was prepared by saturation of chemically pure sulfuric acid with gaseous sulfur trioxide in a special apparatus. Benzene was purified by distillation and freezing until the product with f. p. 5.5° had been reached. Benzenemonosulfonic acid and disulfonic acid were obtained by water hydrolysis of the respective chlorides with m.p. 14.5° and 63°. Water and hydrogen chloride were then removed under vacuum. Sodium sulfate was anhydrous, chemically pure grade.

The amount of sulfone sulfonic acids in the sulfonation mixture was determined on the basis of different solubilities of the sulfonyl chlorides of benzene-m-disulfonic acid and diphenylsulfone-3,3'-disulfonic

acidin ligroine.* Later, after we had developed a polarographic method of determination of sulfone sulfonic acids directly in the sulfonation mixtures, we began to use the latter method almost exclusively owing to its rapidity and greater accuracy [1]. Both analytical methods gave the same results.

Determination of the Character of the Reactions Leading to the Formation of Diphenylsulfonesulfonic Acids.

Isolation of diphenylsulfone formed in the sulfonation of benzene with oleum as an intermediate for the formation of diphenylsulfonedisulfonic acid.

Experiment 1. 20.2 g of benzene was added dropwise at room temperature to 79 g of 66.5% oleum. The sulfonation mixture was poured into about 500 ml of water after stirring for several minutes. The separated diphenylsulfone was filtered off, washed on a Buchner funnel until free of acid and dried. Yield: 1.0 g, m.p. 117°. M. p. after recrystallization from ethyl alcohol was 124-124.5°, which agreed with the literature data.

Experiment 2. 30 g of 66.5% oleum was added dropwise at room temperature to 100 g of benzene. Then the reaction mixture was stirred for three hours and was poured into 120 ml of water. Excess benzene was distilled off (72.64 g). Diphenylsulfone was filtered from the mother liquor, washed with water and dried. Diphenylsulfonesulfonic acids were determined in the filtrate by the polarographic method. 5.74 g of diphenylsulfone was isolated (m.p. 123.5°), i.e., 15% based on reacted benzene. The diphenylsulfonesulfonic acids were not detected.

Experiment 3. Sulfonation of benzenemonosulfonic acid with high concentration oleum. 5 g of 98.88% benzenemonosulfonic acid was introduced into 5.75 g of 66.5% oleum at the temperature of about 20°. Then the temperature of the reaction mixture was raised rapidly to 90° and kept at 90° for three hours. 15.09% of DPS was detected in the sulfonation mixture by the polarographic method, calculated on the charged amount of the benzenemonosulfonic acid.

Experiment 4. Sulfonation of benzenemonosulfonic acid with 20% oleum. 5 g of 98.88% benzenemonosulfonic acid was added to 18.85 g of 21% oleum at the temperature of about 20°. Then the reaction mixture temperature was raised rapidly to 90° and kept at 90° for three hours. 4.5% of DPS was detected in the sulfonation mixture by the polarographic method, calculated on the charged benzenemonosulfonic acid.

Experiment 5. Treatment of benzene-m-disulfonic acid with high concentration oleum. 5 g of 96.38% benzene-m-disulfonic acid was added to 5 g of 66.5% oleum at the temperature of about 20°.. Then the reaction mixture temperature was raised rapidly to 90° and was kept at 90° for three hours. No diphenylsulfonesulfonic acids were detected by the polarographic method in the sulfonation mixture.

Experiment 6. Treatment of benzene with high concentration oleum. * *

Effect of SO₃ Concentration in the Sulfonating Agent on the Degree of Formation of DPS

Benzene was added to oleum at 30-40°; then the temperature was raised over two hours to 90° and was kept at 90° for three hours. As had been shown, benzene is transformed under these conditions completely into benzenedisulfonic acid [1]. The DPS was directly isolated in the form of its chloride in this series of experiments. The results of the experiments are given in Table 2.

Sulfonation of Benzene with Alteration of Conditions at the First Stage — Formation of Benzenemonosulfonic Acid.

Experiment 14. Two-step sulfonation of benzene with 100% sulfuric acid and with 65% oleum. Stage 1.

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*About 1 g of the sulfonyl chloride was placed in a Schott crucible No. 2 and washed with 1 liter of ligroine (fraction with b. p. 70-100°). The chloride of benzene-m-disulfonic acid dissolved in ligroine and passed into the filtrate while the chloride of diphenylsulfone-3,3'-disulfonic acid remained on the filter.

**The experiment was taken from previously published work [1].

60 g of benzene was added to 151 g of 100% sulfuric acid over two hours at 50°. The temperature was raised over three hours to 100° from 50° and was kept at 100° for three hours. Stage 2. 234 g of 64.5 g 64.5% oleum was introduced over three hours into the sulfonation mixture from the first stage while the temperature was uniformly raised from 30° to 80°. A two hour hold at 80° was given. 1.71% of DPS, calculated on benzene charged, was found in the sulfonation mixture.

Experiment 15. Two-step sulfonation of benzene with 20% and 65% oleum. Stage 1. 50.3 g of benzene was added over two hours at 35-55° to 116-85 g of 20% oleum, then the temperature was raised to 90° over two hours and was kept for one hour at 90°. Stage 2. 155.3 g of 65.3% oleum was added over on hour at 30° to the resulting sulfonation mixture, the temperature was raised rapidly to 90° and was kept at 90° for three hours. 14.32% of DPS was found in the sulfonation mixture, calculated on benzene charged.

Effect of Sodium Sulfate on the Degree of Formation of DPS

TABLE 2

No. of expt.	Content of SO_3 in oleum used for the sulfonation (in %)	Number of moles of SO_3 per mole of benzene	Content of diphenylsulfone-3,3'-disulfonic acid in the sulfonation mixture, based on benzene (in %)
7	4.15	2.49	1.1
8	10.0	2.49	1.85
9	17.15	2.51	2.74
10	28.0	2.45	13.24
11	39.55	2.47	13.28
12	48.0	2.49	15.28
6	64.5	2.50	24.26
13	70.3	2.50	31.17

The necessary amount of sodium sulfate was added to the oleum, the temperature being prevented from rising above 25-30° (external cooling). Then the reaction mixture was stirred at the temperature close to 25° (in case of addition of 0.5 mole of sodium sulfate per mole of benzene being sulfonated, at the temperature of about 60°) for 1.5 hours until a uniform mass of the sulfate and the oleum had formed (in case of small amouts

TABLE 3

Expt. No.	SO_3 content in the oleum used for sulfonation (%)	No. of moles of SO_3 per mole of benzene	No. of moles of sodium sulfate per mole of benzene	Temperature of the hold	Duration of the hold (in hours)	Cont. of DPS in the sulfonation mixture, calculated on benzene *(in %)
6	64.5	2.50	--	90°	3	24.2
16	65.3	2.56	0.01	90	3	21.3
17	65.0	2.51	0.05	90	3	15.1
18	66.0	2.48	0.10	90 / 120	1 / 2	9.8
19	66.0	2.50	0.25	90 / 120	1 / 2	5.5
20	65.2	2.43	0.50	90 / 160	3 / 3	1.7

*Diphenylsulfone-3,3'-disulfonic acid was determined in the sulfonation mixture in all experiments of this series by isolation in the form of its sulfonyl chloride

of the sulfate — until its dissolution). Then, benzene was added dropwise at the temperature not higher than 40°. After that the temperature within the flask was raised over two hours to the predetermined level and was kept at that level. The temperature of the hold was different for the various runs depending on the amount of sodium sulfate used. The experimental data are given in Table 3.

SUMMARY

1. It was shown that the formation of diphenylsulfonesulfonic acids during the sulfonation of benzene with oleum proceeds both with the intermediate formation of diphenylsulfone and directly from benzenemono-

sulfonic acid. Benzene-m-disulfonic acid is practically unchanged into the diphenylsulfonesulfonic acids under the conditions used for the sulfonation.

2. Conditions were found under which a minimum formation of diphenylsulfonesulfonic acids is formed.

3. The hindering action of sodium sulfate on the process of formation of diphenylsulfonesulfonic acids was established in the sulfonation of benzene with oleum.

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C-ARYLOXY-P,P-DIMETHOXY-ISOPHOSPHAZOACYLS AND MIXED
# TRIARYLOXY-ISOPHOSPHAZOACYLS

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It was shown in the previous paper [1] that C-chloro-P,P-dimethoxy-isophosphazoacyls and C-chloro-P,P-diaryloxy-isophosphazoacyls (I) are formed according to the following scheme in the reaction of phosphorus pentachloride with diesters of acylamidophosphoric acids:

$$RCONHPO(OR')_2 + PCl_5 \rightarrow POCl_3 + HCl + RCCl{=}NPO(OR')_2.$$
$$(I)$$
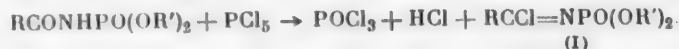
In their chemical nature substances (I) are chlorides of diesters of N-phosphoric acid derivatives of imino acids and therefore possess the properties of esters of N-substituted amidophosphoric acids on one hand and the properties of chlorides of N-substituted iminocarboxylic acids on the other hand. It was of interest to determine whether or not it is possible to prepare C-aryloxy-P,P-dimethoxy-isophosphazoacyls and mixed triaryloxy-isophosphazoacyls of type (II) by aryloxylation of these compounds according to the following scheme:

$$RCCl{=}NPO(OR')_2 + R''ONa \rightarrow NaCl + RC(OR''){=}NPO(OR')_2.$$
$$(II)$$
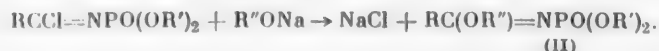
Compounds of type (II) have been unknown until this time and their synthesis by other methods has many great difficulties. It was also of interest to test these compounds as insecticides.

An experiment showed that synthesis of (II) occurs very readily. On mixing the equivalent amounts of sodium p-chlorophenoxide and C-chloro-P,P-dimethoxy-isophosphazoacyls in benzene solution, the reaction proceeds with a rather strong heat evolution and is complete in 5-10 minutes. The reaction of sodium p-chlorophenoxide and C-chloro-P,P-di-p-nitrophenoxy-isophosphazoacyls or sodium p-nitrophenoxide and C-chloro-P,P-diaryloxy-isophosphazoacyls proceeds somewhat more difficultly and it is necessary to reflux the reaction mixture for 2-3 hours in order to complete the reaction.

All mixed triaryloxy-isophosphazoacyls are obtained in the crystalline state directly after the removal of the solvent. C-Aryloxy-P,P-dimethoxy-isophosphazoacyls are obtained in the majority of cases in the form of oils which crystallize wholly or in part after a treatment with solvents and rubbing with a glass rod, the crystallization occurring rapidly.

In their chemical properties (II) are quite similar to triaryloxy-isophosphazoacyls with the same ester groups [2]. Just like these, they are not hydrolyzed by being boiled with water, are very slowly hydrolyzed on being boiled with aqueous alkali solutions, but are readily hydrolyzed on being heated on aqueous alcoholic solutions of alkalies, according to the following scheme

$$RC(OR''){=}NPO(OR')_2 + OH^- \rightarrow R''OH + [RCONPO(OR')_2]^-.$$

This is explained by the fact that (II), like triaryloxyphosphazosulfonylaryls [3] and triaryloxy-isophosphazocyls [2], are very difficultly soluble in water and comparatively readily soluble in alcohol.

The solubility and the melting points of (II), like those of triaryloxy-isophosphazoacyls, depend more on the nature of the ester groups than on the nature of the aryl group connected to the carbonyl carbon atom.

Several (I), previously undescribed in the literature, were prepared as the starting materials for the preparation of mixed triesters. These were prepared by the previously described method [1] from diesters of the corresponding acylamidophosphoric acids and phosphorus pentachloride. All substances (I) prepared by us were low-melting crystalline compounds, readily soluble in benzene and acetone, difficultly in ether and petroleum ether. They are quantitatively converted into the original diesters of acylamidophosphoric acids on being shaken with water or on storage in air, this confirming their structures. These substances titrate with two equivalents to phenolphthalein indicator after a hydrolysis in aqueous alcoholic solutions.

The mixed triaryloxy-isophosphazoacyls do not possess any insecticidal properties. C-p-Nitrophenoxy-P,P-dimethoxy-isophosphazobenzoyl is a rather active contact insecticide. All the remaining C-aryloxy-P,P-dimethoxy-isophosphazoacyls are weak contact insecticides.

EXPERIMENTAL

C-Aryloxy-P,P-dimethoxy-isophosphazoacyls (III). 0.0105 mole of powdered dry sodium phenoxide was rapidly added to a solution of 0.01 mole of C-chloro-P,P-dimethoxy-isophosphazoacyl in 20 ml of benzene with energetic stirring. The reaction mixture warms up considerably owing to the heat of reaction. Stirring was continued until the acid test with Congo red vanished in a sample obtained by the addition of 2-3 drops of water to a drop of the reaction mixture. Usually the acid reaction vanishes after stirring for 10-15 minutes, but in the case of the preparation of C-p-nitrophenoxy-P,P-dimethoxy-isophosphazoacyls, it was necessary to reflux the reaction mixture for 1-2 hours. The reaction mixture was washed with water (2 × 15 ml) in order to remove sodium chloride, the benzene solution was dried with sodium sulfate and the benzene was distilled off under a vacuum. A dense crystalline mass or a viscous oil remained as the residue, and the oil crystallized after the addition of 1-2 drops of petroleum ether and rubbing with a glass rod. Some of the (III) crystallized only very slowly. All (III) are rather readily soluble in benzene and acetone, less readily in ether and alcohol, and very difficultly soluble in petroleum ether and carbon tetrachloride.

C-p-Chlorophenoxy-P,P-dimethoxy-isophosphazobenzoyl: prisms (from a mixture of benzene and petroleum ether); m. p. 85-87°; yield: 63.6%.

Found %: Cl 10.68. $C_{15}H_{15}O_4NPCl$. Calculated %: Cl 10.43.

C-p Nitrophenoxy-P,P-dimethoxy-isophosphazobenzoyl: prisms (from benzene); m. p. 131-133°; yield: 30.0%.

Found %: N 8.06. $C_{15}H_{15}O_6N_2P$. Calculated %: N 7.99.

C-p-Chlorophenoxy-P,P-dimethoxy-isophosphazo-p-chlorobenzoyl: prisms (from benzene); m. p. 112-114°; yield: 30.6%.

Found %: P. 7.92. $C_{15}H_{14}O_4NPCl_2$. Calculated %: P 8.27.

C-p-Nitrophenoxy-P,P-dimethoxy-isophosphazo-p-chlorobenzoyl: prisms (from benzene); m. p. 131-133°; yield: 31.1%.

Found %: P 8.10. $C_{15}H_{14}O_6N_2PCl$. Calculated %: P 8.05.

C-p-Chlorophenoxy-P,P-dimethoxy-isophosphazo-p-nitrobenzoyl: needles (from a mixture of benzene and petroleum ether); m. p. 140-142°; yield 30%.

Found %: N 7.28. $C_{15}H_{14}O_5N_2PCl$. Calculated %: N 7.09.

C-p-Nitrophenoxy-P,P-dimethoxy-isophosphazo-p-nitrobenzoyl: prisms (from benzene); m.p. 128-130°; yield: 33.9%.

Found %: N 10.80. $C_{15}H_{14}O_8N_3P$. Calculated %: N 10.63.

C-p-Chlorophenoxy-P,P-dimethoxy-isophosphazo-m-nitrobenzoyl: prisms (from benzene); m.p. 145-147°; yield: 70.0%.

Found %: N 6.95. $C_{15}H_{14}O_6N_2PCl$. Calculated %: N 7.09.

C-p-Nitrophenoxy-P,P-dimethoxy-isophosphazo-m-nitrobenzoyl: prisms (from benzene); m.p. 126-128°; Yield: 54.4%.

Found %: N 10.68. $C_{15}H_{14}O_8N_3P$. Calculated %: N 10.63.

C-p-Chlorophenoxy-P,P-dimethoxy-isophosphazo-3,5-dinitrobenzoyl: prisms (from a mixture of benzene and petroleum ether); m.p. 100-103°; yield: 44.4%.

Found %: N 9.80. $C_{15}H_{13}O_8N_3PCl$. Calculated %: N 9.77.

C-p-Nitrophenoxy-P,P-dimethoxy-isophosphazo-3,5-dinitrobenzoyl: prisms (from benzene); m. p. 151-153°; yield: 73.4%.

Found %: N 13.03. $C_{15}H_{13}O_{10}N_4P$. Calculated %: N 12.73.

C-Aryloxy-P,P-diphenoxy-isophosphazoacyls (IV). These were prepared like (III). All (IV) were rather readily soluble in acetone and benzene, less readily in alcohol and ether and very difficultly in petroleum ether and carbon tetrachloride.

C-p-Chlorophenoxy-P,P-diphenoxy-isophosphazobenzoyl: prisms (from a mixture of benzene and petroleum ether); m.p. 124-126°; yield: 80.0%.

Found %: Cl 7.81. $C_{25}H_{19}O_4NPCl$. Calculated %: Cl 7.66.

C-p-Nitrophenoxy-P,P-diphenoxy-isophosphazobenzoyl: prisms (from benzene); m. p. 157-159°; yield: 95.4%.

Found %: N 5.98. $C_{25}H_{19}O_2N_2P$. Calculated %: N 5.90.

C-p-Chlorophenoxy-P,P-diphenoxy-isophosphazo-p-chlorobenzoyl: prisms (from benzene); m. p. 143-145°; yield: 100%.

Found %: Cl 14.56. $C_{25}H_{18}O_4NPCl_2$. Calculated %: Cl 14.22.

C-p-Nitrophenoxy-P,P-diphenoxy-isophosphazo-p-chlorobenzoyl: needles (from benzene); m. p. 155-157°; yield: 81.0%.

Found %: Cl 6.99. $C_{25}H_{18}O_6N_2PCl$. Calculated %: Cl 6.96.

C-p-Chlorophenoxy-P,P-diphenoxy-isophosphazo-p-nitrobenzoyl: prisms (from benzene); m.p. 118-120°; yield: 68.8%.

Found %: Cl 6.98. $C_{25}H_{18}O_6N_2PCl$. Calculated %: Cl 6.98.

C-p-Nitrophenoxy-P,P-diphenoxy-isophosphazo-p-nitrobenzoyl: prisms (from benzene); m. p. 162-164°; yield: 55.6%.

Found %: N 8.70. $C_{25}H_{18}O_7N_3P$. Calculated %: N 8.34.

C-p-Chlorophenoxy-P,P-diphenoxy-isophosphazo-m-nitrobenzoyl: prisms (from benzene); m. p. 124-126°; yield: 60.9%.

Found %: Cl 7.08. $C_{25}H_{18}O_6N_2PCl$. Calculated %: Cl 6.98.

C-p-Nitrophenoxy-P,P-diphenoxy-isophosphazo-m-nitrobenzoyl: prisms (from a mixture of benzene and petroleum ether); m. p. 128-130°; yield: 99.9%.

Found %: N 8.08. $C_{25}H_{18}O_8N_3P$. Calculated %: N 8.08.

C-p-Chlorophenoxy-P,P-diphenoxy-isophosphazo-3,5-dinitrobenzoyl: prisms (from benzene); m. p. 181-183°; yield: 79.6%.

Found %: N 7.48. $C_{25}H_{17}O_8N_3PCl$. Calculated %: N 7.58.

C-p-Nitrophenoxy-P,P-diphenoxy-isophosphazo-3,5-dinitrobenzoyl: prisms (from benzene); m. p. 204-206°; yield: 68.9%.

Found %: N 9.96. $C_{25}H_{17}O_{10}N_4P$. Calculated %: N 9.92.

C-p-Nitrophenoxy-P,P-di-p-chlorophenoxy-isophosphazoacyls (V). 0.0105 mole of thoroughly powdered dry sodium p-nitrophenoxide was added with stirring to a solution of 0.01 mole of C-chloro-P,P-di-p-chlorophenoxy-isophosphazoacyl in 30 ml of benzene and the mixture was refluxed until the acid reaction to Congo red in a test with water disappeared, for which 1-3 hours were required. Sodium chloride was washed away with water (2 x 20 ml); part of the product precipitated in the crystalline state at this juncture. Benzene was distilled off under vacuum for a more complete isolation of the substance. Substances (V) were rather readily soluble in acetone, less readily in benzene and dioxane and very difficultly in ether, petroleum ether and carbon tetrachloride.

C-p-Nitrophenoxy-P,P-di-p-chlorophenoxy-isophosphazobenzoyl: prisms (from benzene); m. p. 142-144°; yield: 85.4%.

Found %: Cl 13.01. $C_{25}H_{17}O_6N_2PCl_2$. Calculated %: Cl 13.05.

C-p-Nitrophenoxy-P,P-di-p-chlorophenoxy-isophosphazo-p-chlorobenzoyl: prisms (from a mixture of benzene and petroleum ether); m. p. 151-153°; yield: 79.2%.

Found %: Cl 17.94. $C_{25}H_{16}O_6N_2PCl_3$. Calculated %: Cl 18.42.

C-p-Nitrophenoxy-P,P-di-p-chlorophenoxy-isophosphazo-p-nitrobenzoyl: needles (from benzene); m.p. 162-164°; yield: 88.4%.

Found %: N 7.03. $C_{25}H_{16}O_8N_3PCl_2$. Calculated %: N 7.13.

C-p-Nitrophenoxy-P,P-di-p-chlorophenoxy-isophosphazo-p-nitrobenzoyl: prisms (from benzene); m.p. 133-135°; yield: 85.0%.

Found %: N 7.09. $C_{25}H_{16}O_8N_3PCl_2$. Calculated %: N 7.13.

C-p-Nitrophenoxy-P,P-di-p-chlorophenoxy-isophosphazo-3,5-dinitrobenzoyl: prisms (from a mixture of benzene and dioxane); m. p. 209-210°; yield: 77.6%.

Found %: N 9.62. $C_{25}H_{15}O_{10}N_4PCl_2$. Calculated %: N 9.36.

C-p-Chlorophenoxy-P,P-di-p-nitrophenoxy-isophosphazoacyls (VI) were prepared like (V). Substances (VI) were rather readily soluble in acetone, less readily in benzene and dioxane and very difficultly in ether, petroleum ether and carbon tetrachloride.

C-p-Chlorophenoxy-P,P-di-nitrophenoxy-isophosphazobenzoyl: prisms (from dioxane); m. p. 180-182°; yield: 69.3%.

Found %: N 7.94. $C_{25}H_{17}O_8N_3PCl$. Calculated %: N 7.58.

C-p-Chlorophenoxy-P,P-di-p-nitrophenoxy-isophosphazo-p-chlorobenzoyl: plates (from a mixture of benzene and petroleum ether); m.p. 139-141°; yield: 73.6%.

Found %: N 7.08. $C_{25}H_{16}O_8N_3PCl_2$. Calculated %: N 7.13.

C-p-Chlorophenoxy-P,P-di-p-nitrophenoxy-isophosphazo-p-nitrobenzoyl: Needles (from dioxane); m.p. 217-219°; yield: 66.9%.

Found %: N 9.16. $C_{25}H_{16}O_{10}N_4PCl$. Calculated %: N 9.35.

C-p-Chlorophenoxy-P,P-di-p-nitrophenoxy-isophosphazo-m-nitrobenzoyl: prisms (from benzene); m. p. 149-151°; yield: 50.2%.

Found %: N 9.37. $C_{25}H_{16}O_{10}N_4PCl$. Calculated %: N 9.35.

C-p-Chlorophenoxy-P,P-di-p-nitrophenoxy-isophosphazo-3,5-dinitrobenzoyl: prisms (from dioxane); m.p. 200-202°; yield: 76.6%.

Found %: N 10.73. $C_{25}H_{15}O_{12}N_5PCl$. Calculated %: N 10.87.

C-Chloro -P,P-diaryloxy-isophosphazoacyls were prepared by the previously described method [1].

C-Chloro-P,P-di-p-chlorophenoxy-isophosphazo-m-nitrobenzoyl: prisms, m. p. 120-123°; yield: 80.1%.
Found: equivalents after hydrolysis 1.98. $C_{19}H_{12}O_5N_2PCl_3$. Calculated: equivalents after hydrolysis 2.00.

C-Chloro-P,P-di-p-nitrophenoxy-isophosphazo-m-nitrobenzoyl: prisms, m. p. 130-131°; yield: 90.0%.
Found: equivalents after hydrolysis 1.98. $C_{19}H_{12}O_9N_4PCl$. Calculated equivalents after hydrolysis 2.00.

C-Chloro-P,P-di-p-chlorophenoxy-isophosphazo-3,5-dinitrobenzoyl: prisms, m.p. 128-130°; yield: 79.1%.
Found: equivalents after hydrolysis 1.99. $C_{19}H_{11}O_7N_3PCl_3$. Calculated: equivalents after hydrolysis 2.00.

C-Chloro-P,P-di-p-nitrophenoxy-isophosphazo-3,5-dinitrobenzoyl: prisms, m.p. 55-57°; yield: 90.0%.
Found: equivalents after hydrolysis 2.02. $C_{19}H_{11}O_{11}N_5PCl$. Calculated: equivalents after hydrolysis 2.00.

Hydrolysis of C-p- nitrophenoxy-P,P-diphenoxy-isophosphazoacyls (IV). A mixture of 0.001 mole of (IV), 60 ml of alcohol and 10 ml of 0.2 N aqueous sodium hydroxide solution was refluxed for one hour. During this time the precipitate dissolved completely. The alcohol was distilled off under vacuum and 5 ml of water and 5 N hydrochloric acid were added to the residue to the acid test with Congo red. The diester precipitated thereupon in the form of an oil, which soon crystallized. They were filtered off, washed with water and alcohol and were crystallized. Yield: 60-70%. The diesters were identified by mixed melting points with authentic diesters of acylamidophosphoric acids.

SUMMARY

A series of C-aryloxy-P,P-dimethoxy-isophosphazoacyls and a series of mixed triaryloxy-isophosphazo-acyls were prepared by the action of sodium aryloxides on C-chloro-P,P-dimethoxyphosphazoacyls and C-chloro-P,P-di-aryloxy-isophosphazo acyls, and their properties were described. It was shown that the diaryl esters of acylamidophosphoric acids are formed in the alkaline hydrolysis of mixed triaryloxy-isophosphazoacyls.

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# CONCERNING THE REACTIONS OF TRIMETHYLACETOXYSILANE WITH TETRABUTOXYTITANIUM AND TITANIUM TETRACHLORIDE

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The condensation reactions of alkylacetoxysilanes with tetrabutoxytitanium and titanium tetrachloride have not been studied to this date. At the same time, the reactions of heterofunctional condensation of esters and alkylhalosilanes with alkyl- and arylacetoxysilanes proceed readily and lead to the formation of various monomeric and polymeric organosilicon compounds [1]. It was of considerable interest to determine the possibility of applications of this method to the synthesis of mixed organotitaniumsilicon compounds. We expected to obtain tetrakis-(trimethylsiloxy)-titanium in the condensation of trimethylacetoxysilane with tetrabutoxytitanium, according to the following scheme:

$$4(CH_3)_3SiOCOCH_3 + Ti(OC_4H_9)_4 \rightarrow Ti[OSi(CH_3)_3]_4 + 4CH_3COOC_4H_9.$$

However, the experiments showed that this reaction evidently has only a secondary significance. This is confirmed by the fact that we failed to prepare tetrakis-(trimethylsiloxy)-titanium in the condensation of tetrabutoxytitanium with trimethylacetoxysilane. We did obtain some solid, colorless infusible substances which decomposed on being heated to a high temperature and which were soluble in hot alcohol. The examination of the elemental composition of these products, the determination of the acetoxy group content and that of the molecular weight showed that the experimental analytical data corresponded to octaacetoxycyclotetratitanoxane (I) and heptaacetoxytrimethylsiloxycyclotetratitanoxane (II).

$$[TiO(OCOCH_3)_2]_4 \quad [(CH_3COO)_2TiO]_3OTi{<}^{OCOCH_3}_{OSi(CH_3)_3}$$

$$(I) \qquad\qquad (II)$$
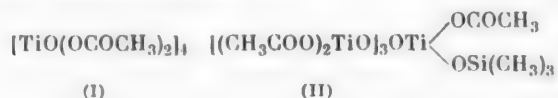
The structure of (I) was also confirmed by its examination via the infrared spectra. A study of product (I) in anhydrous alcohol solution showed that it had an absorption band which corresponded to that of the acetate group in the 2-14μ region of the infrared spectrum. The frequency of the maximum of the absorption band was somewhat higher relative to the frequency of the acid, from 1662 to 1698 cm^{-1}, which is evidently explained by the effect of the titanium atom.

Compounds (I) and (II) do not melt on being heated to 340°, but they begin to darken and decompose at this temperature. They are readily soluble in hot ethyl alcohol and are insoluble in gasoline, benzene, toluene, chlorobenzene, acetone and amyl acetate. Consequently, the main reaction between trimethylacetoxysilane and tetrabutoxytitanium proceeds in the direction of replacement of the butoxy groups by acetoxy groups with formation of polymers with cyclic structure.

The reaction of substitution of chlorine in titanium tetrachloride by the acetoxy groups and the formation of a polymeric product occur in the condensation of trimethylacetoxysilane with titanium tetrachloride, just as in the case of the condensation of trimethylacetoxysilane with tetrabutoxytitanium. The reaction leading to the formation of compounds with Ti-O-Si bonds occurs with difficulty and again we failed to isolate the tetrakis-(trimethylsiloxy)-titanium. Solid colorless products are formed in the reaction of trimethylacetoxysilane with titanium tetrachloride. Their formation begins at room temperature after addition of titanium tetra-

chloride to trimethylacetoxysilane. The amount of solid products increases on heating. A solid colorless substance which did not melt on being heated to 300°, but was decomposed at this temperature, was isolated during the examination of the reaction products. This was readily soluble in hot ethyl alcohol and insoluble in gasoline, benzene, toluene, chlorobenzene, acetone and amyl acetate. The substance may be purified only with difficulty. The analytical data of this product correspond to a structure that is close in composition to $C_{11}H_{21}O_{12}ClSiTi_3$.

EXPERIMENTAL

Starting materials. Tetrabutoxytitanium: b. p. 203-204° (30 mm), $n^{20}D$ 1.3915, titanium content 14.2% (calculated 14.1%). Prepared by the method described in the literature [2]. Trimethylacetoxysilane: acetoxy group content: 44.5% (calculated 44.7%). Prepared by heating trimethylchlorosilane with sodium acetate for five hours at 35-40°. The product was distilled through a fractionating column with 16 theoretical-plate efficiency. B. p. 102-103°, $n^{20}D$ 1.3890. Titanium tetrachloride: chemically pure, b.p. 136.5°.

Condensation of Trimethylacetoxysilane with Tetrabutoxytitanium

Experiment 1. 48.3 g of trimethylacetoxysilane was placed into a four-necked flask with a stirrer, a thermometer, a reflux condenser and a dropping funner, heated to 75° and treated with stirring with 16.58 g of tetrabutoxytitanium. A colorless solid product formed after the addition of tetrabutoxytitanium. The reaction mixture was then heated for five hours at 92-94°. The liquid part was distilled under vacuum after the completion of the reaction. The solid product was washed with ether and dried. The weight of the product was 9.5 g. The solid product was soluble in hot alcohol and insoluble in gasoline, benzene, toluene, chlorobenzene, cellosolve, acetone and amyl acetate.

Found %: Ti 26.37, 26.93; C 27.36, 27.32; H 4.02, 4.03; CH_3COO 65.03 M (in phenol) 742. $C_{16}H_{24}O_{20}Ti_4$. Calculated %: Ti 26.33; C 26.39, H 3.29; CH_3COO 64.87. M 728.

24.6 g of trimethylacetoxysilane (b. p. 102.5-103°, $n^{20}D$ 1.3885) and 10.5 g of butyl acetate (b.p. 123.5-124.5°, $n^{20}D$ 1.3950) was isolated after the distillation of the liquid part which was distilled from the solid reaction product.

The determination of the acetoxy group content in the reaction product was run by two methods: 1) boiling of a sample with 0.1N alkali solution with subsequent titration of excess alkali by 0.1N sulfuric acid solution, and 2) solution of a sample in anhydrous alcohol and titration of this solution with 0.1N alcoholic alkali solution. The content of the acetoxy groups in trimethylacetoxysilane was determined by boiling a sample with 0.1N alkali solution with a subsequent titration of excess alkali with 0.1N sulfuric acid solution. For the determination of the acetoxy groups in butyl acetate, the latter was hydrolyzed by 0.5 N alcoholic alkali solution.

Experiment 2. 78 g of trimethylacetoxysilane was placed into the reaction flask, heated to 75° and treated with stirring with 24.9 g of butyl orthotitanate. Then the mixture was heated to 92-94° for five hours. A solid colorless product and a liquid with a strong odor of butyl acetate formed after 30 minutes after the addition of the butyl ester. The liquid part was vacuum distilled. The solid colorless product was washed with ether (3 times, 100 ml each), and dried in vacuum. The weight of the product was 13 g. This was soluble in hot ethyl and butyl alcohols, insoluble in gasoline, benzene, toluene, chlorobenzene, cellosolve, acetone and amyl acetate.

Found %: Ti 25.17, 24.91; Si 4.00, 4.01; C 27.3, 27.45; H 3.92, 4.10; CH_3COO 56.6, 56.3. $C_{17}H_{30}O_{19}SiTi_4$. Calculated %: Ti 25.29; Si 3.69; C 26.92; H 3.95; CH_3COO 54.51.

40 g of trimethylacetoxysilane (b.p. 103°, $n^{20}D$ 1.3886) and 16 g of butyl acetate (b.p. 123.5-124.5°, $n^{20}D$ 1.3950) were isolated during the distillation of the liquid part, distilled from the solid reaction product.

Condensation of Trimethylacetoxysilane with Titanium Tetrachloride

42.9 g of trimethylacetoxysilane was placed into a flask with a stirrer, a thermometer, a dropping funnel and a lead-off tube connected to a receiver for volatile liquid reaction products, and 4.56 g of titanium tetrachloride was introduced with stirring from the dropping funnel. A colorless solid product precipitated immediately. Then the reaction mixture was heated to 83° and over one hour at this temperature there distilled 2.62 g

of a colorless liquid. A colorless solid product and a liquid, which was then distilled off under vacuum, were left in the flask after the completion of the reaction. The colorless solid product was washed with ether (3 times, 100 ml each). The weight of the dry product was 3.2 g. It was soluble in hot anhydrous alcohol, insoluble in benzene, toluene, chlorobenzene, gasoline, acetone and amyl acetate.

Found %: Ti 28.37, 28.10; Si 6.77, 6.58; C 20.0, 20.03; H 3.56, 3.60; Cl 9.62, 9.80; CH_3COO. 44.5, 44.35. $C_{11}H_{21}O_{12}ClSiTi_4$. Calculated %: Ti 26.02; Si 5.07; C 23.91; H 3.6; Cl 6.42; CH_3COO 42.74.

The liquid which was distilled from the solid reaction product was trimethylacetoxysilane (b. p. 102-103°, $n^{20}D$ 1.3890).

The volatile liquid products which distilled during the condensation reaction consisted of a mixture of trimethylchlorosilane and acetyl chloride:

B. p. 54-57°, d^{20}_4 0.8670, $n^{20}D$ 1.3887.
Found %: Cl 21.51, 22.0; CH_3COO 24.0, 23.8; Si 23.55, 23.73.

Hexamethyldisiloxane [b. p. 99.5° (750 mm), $n^{20}D$ 1.3750; silicon content 33.75%] was isolated after hydrolysis of the volatile products with b. p. 54-57° with water.

The content of the acetoxy groups and of chlorine in the solid reaction product, in the liquid portion and in the volatile liquid reaction products was determined as follows: a sample of 0.1-0.2 g was boiled for 20 minutes with 10-20 ml of 0.1N alkali solution, after which excess alkali was titrated with 0.1N sulfuric acid solution. Having determined the total content of acetoxy groups and chlorine in this manner, we determined the content of chlorine by the Volhard method, in the same sample.

SUMMARY

1. The condensation of trimethylacetoxysilane with tetrabutoxytitanium does not lead to formation of tetrakis-(trimethylsiloxy)-titanium, but is accompanied by the replacement of the butoxy groups by acetoxy groups at the titanium atom and leads to the formation of cyclic compounds: octa-acetoxycyclotetratitanox-ane and heptaacetoxy-(trimethylsiloxy)-cyclotetratitanoxane.

2. The condensation of trimethylacetoxysilane with titanium tetrachloride leads to replacement of the halogen atoms at the titanium atom by acetoxy groups.

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CONCERNING THE TAUTOMERISM OF ACYL DERIVATIVES OF 2-AMINOTHIAZOLE

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The acetylation product of 2-phenylamino-4-methylthiazole became necessary in the course of a study of the phenomenon of tautomerism among the derivatives of 2-aminothiazole. An examination of the literature revealed that two different acetyl derivatives of this amine have been described. One compound with m.p. 114° was prepared by Young and Crooks [1] in 1906 by acetylation of the amine with acetic anhydride in the presence of sodium acetate, while the other compound with m.p. 174° was prepared in 1946 by Hurd and Kharasch [2] by the action of acetic anhydride, with addition of concentrated sulfuric acid, on the amine.

Considering the capability of 2-aminothiazole to react in the amino and the imino forms, it is possible to suppose that isomeric compounds with structures (A) and (B) are formed under different conditions of acetylation, these corresponding to the two tautomeric forms of 2-aminothiazole.

Simultaneously with the checking of this supposition it was of interest to determine to what extent is the ability to form two isomeric acetylation products characteristic of other derivatives of 2-aminothiazole.

2-Arylaminothiazoles (I-V) (Table 1) synthesized for this purpose were acetylated under various conditions (in the presence of sodium acetate and concentrated sulfuric acid). Here for each amine we obtained two acetyl derivatives (a) and (b) (Table 1) depending on the addend used. At the same time, we succeeded in isolating only one acetylation product with m. p. 132-133° * during the acetylation of 2-amino-4-methylthiazole, which is unsubstituted at the amino group. Therefore, it could have been expected that the formation of two isomeric acetyl compounds of 2-arylaminothiazoles is connected with the existence of the phenyl group at the nitrogen atom of the amino group. However, strangely, two isomeric acetyl derivatives were also obtained during the acetylation of the methyl analog (VI) under the same condtions.

The acetyl derivatives prepared in the presence of anhydrous sodium acetate were substances with lower melting points than the isomeric acetyl derivatives obtained in the presence of concentrated sulfuric acid.

It appeared after the refinement of the conditions for running the acetylation reaction, that the presence of sodium acetate was not necessary for the formation of the low-melting isomers. These isomers were obtained also in the absence of any addends. ** The high-melting isomers were formed not only in the presence of

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*As indicated earlier, the acetyl residue in this compound is at the nitrogen atom of the amino group [3].
**As we showed, data given in [2] to the effect that 2-phenylamino-4-methylthiazole is not acetylated on being boiled with acetic anhydride without the addition of sodium acetate, do not correspond to reality.

concentrated sulfuric acid but also in the presence of phosphoric acid or zinc chloride.

Two isomeric acylation products are also formed in the reaction of amine (I) with propionic anhydride. Propionyl derivative (VII) with m. p. 101-103° is formed in acylation of this amine without any addends, while substance (VIII) with m.p.164-166° is formed in the presence of concentrated sulfuric acid.

As mentioned above, the isomeric acetyl derivatives may have the structures (A) and (B). The problem could be solved by the comparison of their properties with substances having the authentic (A) and (B) structures. Substance (A) was to be prepared by the condensation of chloroacetone with 1-phenyl-1-acetylthiourea, while substance (B) — by condensation of 1-phenyl-3-acetylthiourea with chloroacetone. However, the desired results

TABLE 1

Substituted 2-Aminothiazoles and Melting Points of Their Acetyl Derivatives

Amine	X	Y	Acetyl deriva- tive	M. p. of acet- yl derivative
(I)	CH_3	C_6H_5	(a) (b)	115—117° 174—175
(II)	C_6H_5	C_6H_5	(a) (b)	132—133 172—174
(III)	H	C_6H_5	(a) (b)	100—102 215—216
(IV)	CH_3	$p\text{-}C_6H_4Cl$	(a) (b)	129—131 200—202
(V)	CH_3	$p\text{-}C_6H_4OCH_3$	(a) (b)	125—127 146—147
(VI)	CH_3	CH_3	(a) (b)	109—110 141—142

were not attained; 1-phenyl-1-acetylthiourea rearranged very easily into 1-phenyl-3-acetylthiourea in the course of the reaction, and the latter gave with chloroacetone the compound with m.p. 181-182°, which was identical with 3-phenyl-4-methyl-2-acetylimino-4-thiazoline (X). The structures of the high-melting and the low-melting products could be estimated by a comparison of the ultraviolet absorption spectra of these compounds with those of related compounds having the authentic imino structures (IX-XII).
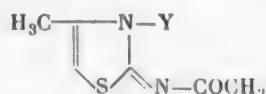
(IX) Y = CH_3, (XI) Y = $p\text{-}C_6H_4Cl$,
(X) Y = C_6H_5, (XII) Y = $p\text{-}C_6H_4OCH_3$.

Compound (IX) was prepared by methylation of 4-methyl-2-acetamidothiazole [4], while compounds (X-XII) were prepared by acetylation of the corresponding 3-aryl-4-methyl-2-imino-4-thiazolines with acetic anhydride; the latter substances were synthesized by Bayer's method [5] by the condensation of chloroacetone with substituted thioureas in an alcoholic medium in the presence of concentrated hydrochloric acid. * Compounds (IX-XII) have the same iminothiazoline skeleton as do compounds with structure (B).

It turned out that the greatest similarity with the spectra of compounds (IX-XII) in the general form of the absorption curves and in the location of the absorption maximum was found in the spectra of the high-melting acetyl derivatives. The absorption maxima of the model compounds (IX-XII) lies at 304-305 mμ. The

—————
*Compounds (XI) and (XII) as well as the starting imines have not been described in the literature (see experimental part).

high-melting isomers (b) show an absorption maximum within the same limits (302-315 mμ), while the low-melting acetyl compounds absorb in the shorter wavelength region of the spectrum and have maxima at 267-275 mμ (Figures 1 and 2). It is possible to conclude from such data and with a considerable degree of certainty that the high-melting isomers have the acylimine structure (B), while the low-melting isomers have that of the acylamide type (A).

The data from the infrared absorption spectra agree with this conclusion as well.[*] The high-melting acetyl compounds produce an intense absorption band at 1689-1681 cm^{-1}, which corresponds to the bond vibration of the carbonyl group in the acetyl residues, while the low-melting acetyl derivatives absorb in the longer wavelength region of the spectrum (1676-1664 cm^{-1}). Usually the carbonyl frequency of the acetyl residue in N,N'-disubstituted amides is located at 1650 cm^{-1}, while with but one substitutent — phenyl — at a somewhat higher frequency [6]. Otting [7] and Staab [8] have shown recently that higher vibration frequencies are characteristic for the carbonyl of the acetyl group bound to a nuclear nitrogen atom, in comparison with the carbonyl of the acetamide residues. The higher frequencies for the carbonyl of the high-melting acetyl compounds indicate the iminothiazoline structure (B) of these compounds. The infrared spectrum data also indicate that in the high-melting acetyl derivatives (structure B) the bond polarization between the ring nitrogen atom and the carbon atom of the carbonyl is greater than it is in the low-melting compounds (structure A). The lower solubility of these compounds in organic solvents and the higher melting points, in comparison with the solubilities of the low-melting compounds and their melting points, are in agreement with this statement.
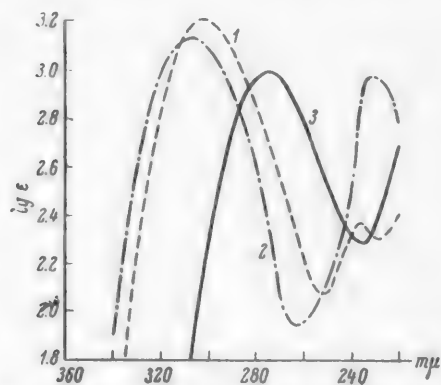

Fig. 1. Ultraviolet absorption spectra. 1) 3-Methyl-4-methyl-2-acetylimino-4-thiazoline (IX), 2) 3-acetyl-4-methyl-2-methylimino-4-thiazoline (VIb), 3) 2-acetylmethylamino-4-methylthiazole (Ia).
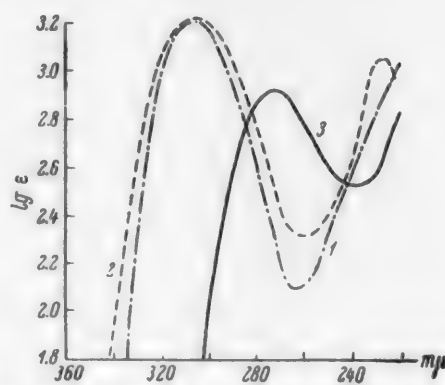
Fig. 2. Ultraviolet absorption spectra. 1) 3-Phenyl-4-methyl-2-acetylimino-4-thiazoline (X), 2) 3-acetyl-4-methyl-2-phenylimino-4-thiazoline (Ib), 3) 2-acetylphenylamino-4-methylthiazole (Ia).

An attempt was made to isomerize acetamides (A) into acetylimines (B) by heating to 10° above the melting point. However, acetamides (A) were not materially changed by this. Similarly, acetylimines (B) failed to suffer an isomerization on being heated above their melting points. The transformation (A) → (B) was attained for 2-acetylphenylamino-4-methylthiazole (Ia) by heating in acetic anhydride, meticulously freed of acetic acid, in the presence of a small amount of sulfuric acid. The isomeric 3-acetyl-4-methyl-2-phenyl-imino-4-thiazoline (Ib) was obtained in good yield in this case. Evidently, in this case a transacetylation — transfer realized through a stage of an addition of the proton of the acid to the ring nitrogen atom — took place, rather than a transition of a less stable isomer into the more stable one.

Some interesting results were obtained on heating the acetyl derivatives with propionic anhydride in the presence of concentrated sulfuric acid. The 2-acetylphenylamino-4-methylthiazole (Ia) was thereby changed into the high melting propionyl derivative. 3-Acetyl-4-methyl-2-phenylimino-4-thiazoline (Ib) gave, under these conditions of the reaction, a mixture of products which could not be separated.

It is interesting that both acetyl derivatives above (Ia and Ib) remain unchanged on being heated with propionic anhydride without the addition of sulfuric acid.

The behavior of the propionyl derivatives is like the acetyl derivatives: the low-melting propionyl derivative(VII) passes into the high-melting isomer (VIII) on being heated with propionic anhydride in the presence of sulfuric acid, while on being heated with acetic anhydride in the presence of sulfuric acid it yields the high-melting acetyl derivative — 3-acetyl-4-methyl-2-phenylimino-4-thiazoline (Ib).

Thus, only 2-acylamido derivatives, which are capable of adding a proton of an acid to the ring nitrogen atom, are subjected to transacylation in the presence of sulfuric acid.

It may be considered, in connection with the complete analogy of behavior, that the propionyl derivatives are constructed like the acetyl derivatives, i.e., the low-melting compound is 2-propionylphenylamino-4-methyl-thiazole (VII), while the high-melting one is 3-propionyl-4-methyl-2-phenylimino-4-thiazoline (VIII). The reactions presented in this paper may be presented, in that case, by the following scheme:
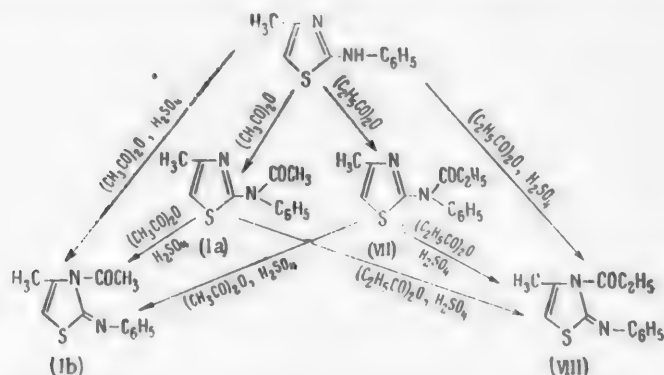
In conclusion, we checked the behavior of some other 2-arylamino heterocycles during acetylation under various conditions. Thus, 2-phenylaminobenzothiazole, 2-phenylaminopyridine and 2-phenylamino-5-methyl-thiodiazole were subjected to acetylation. It turned out that each of these compounds, which was related to 2-phenylaminothiazole, gave the same acetylation product in the presence of sodium acetate, in its absence and in the presence of concentrated sulfuric acid.

Evidently, the formation of two different acetylation products for 2-methyl- and 2-phenylaminothiazole is connected with the specific peculiarities of structure of the thiazole ring in these compounds.

EXPERIMENTAL

Bases (I-VI). 2-Aryl(alkyl)-aminothiazoles (I-IV, VI) were prepared according to the literature data. The melting points of the compounds were: (I) 115-116° (117-118° [1]); (II) 137-138° (139-140° [9]), (III) 121-123° (126° [10]), (IV) 143-143.5° (147° [11]), (VI) 71-72° (71.5-72.5° [1]). The previously undescribed 2-p-methoxyphenylamino-4-methylthiazole (V) was prepared as follows: a suspension of 1.82 g of p-methoxy-phenylthiourea, 0.92 g of chloroacetone and 7.5 ml of water was refluxed for two hours. The cooled solution was neutralized with 30% sodium hydroxide. The resulting precipitate was recrystallized to a constant melting point. It formed prisms of rhombic form (from alcohol); m.p. 99-100.5°. Yield: 1.85 g (84.1%).

Found %: N 12.83. $C_{11}H_{12}ON_2S$. Calculated %: N 12.73.

Acetylation of bases (I-VI) with acetic anhydride. 1) In the presence of anhydrous sodium acetate. A mixture of 2-aryl(alkyl)-aminothiazole, anhydrous sodium acetate (0.2 g of the acetate per 1 g of base) and acetic anhydride (excess) was refluxed for 1.5-2 hours, after which it was poured on ice. The separated product (a) was recrystallized to a constant melting point. The results of the syntheses and the analytical data are given in Table 2.

2) In the presence of concentrated sulfuric acid. A mixture of 2-aryl(alkyl)-aminothiazole, acetic anhydride and concentrated sulfuric acid (0.1 ml of the acid per 1 g of base) was refluxed for 2.5-3 hours, after

TABLE 2

Acetylation Products of Bases (I-VI)

Acetyl derivative	M. p.	Yield (in %)	Empirical formula	% N found	% N calc.	UV λmax	UV lg ε	UV λmin	UV lg ε	UV λmax	UV lg ε	Infrared absorption spectra ****
(Ia)	115—117°[1]	82	$C_{12}H_{12}ON_2S$	—	—	—	—	238	2.45	275	2.91	1676 st, 1618(w), 1592(w), 1566(w), 1547(m), 1502(w), 1422(w), 1335(m), 1312 st
(Ib)	174—175 [2]	69	$C_{12}H_{12}ON_2S$	—	—	229	3.06	266	2.29	307	3.23	1689 st, 1660(m), 1597(w), 1566(w), 1554(w), 1523(m), 1338(m), 1321(w), 1283 st, 1187(w), 1117(w), 1082(w), 1069(w), 1040(m), 1018(w), 1008(w), 993(w)
(IIa)	132—133	80	$C_{17}H_{14}ON_2S$	9.58	9.52	234	3.38	249	3.1	269	3.25	
(IIb)	172—174	57	$C_{17}H_{14}ON_2S$	9.84	9.52	252	3.24	283	2.82	314	3.07	
(IIIa)	100—102	62	$C_{11}H_{10}ON_2S$	12.82	12.84	—	—	235	2.53	267	2.9	
(IIIb)	215—216	50	$C_{11}H_{10}ON_2S$	12.21	12.84	224	2.93	259	2.16	302	3.21	
(IVa)	129—131	73	$C_{12}H_{11}ON_2ClS$	10.8	10.51	—	—	235	2.49	272	2.97	
(IVb)	200—202	62	$C_{12}H_{11}ON_2ClS$	10.53	10.51	222	3.19	260	2.3	304	3.23	
(Va)	125—127	91	$C_{13}H_{14}O_2N_2S$ **	10.79	10.68	225	3.2	249	2.64	275	2.98	
(Vb)	146—147	42	$C_{13}H_{14}O_2N_2S$ ***	11.00	10.68	228	3.29	260	2.35	306	3.22	
(VIa)	109—110[10]	61	$C_7H_{10}ON_2S$	—	—	—	—	235	2.26	274	3.00	1664(st), 1552(m), 1511(st), 1338(m), 1279(m), 1165(m), 1160(m), 1104(w), 1089(w), 1028(w), 1011(m), 980(w)
(VIb)	141—142	57	$C_7H_{10}ON_2S$	16.67	16.47	229	2.98	263	1.95	307	3.14	1753(w), 1681(st), 1530(m), 1425(m), 1318(st), 1268(st), 1215(w), 1157(m), 1093(w), 1043(w), 1012(m), 998(w), 988(w)

*The ultraviolet spectra were taken with the SF-4 spectrophotometer (solutions in alcohol, layer thickness 1 mm, concentration 10^{-3} m).

**Found %: C 59.67, H 5.38. Calculated %: C 59.54, H 5.34.

***Found %: C 59.83, H 5.26. Calculated %: C 59.54, H 5.34.

****The infrared spectra of substances (Ia), (Ib), (VIa) and (VIb) were taken with the recording IKS-11 spectrophotometer, using sodium chloride prisms (2.5-13 m region). The substances were examined in the crystalline state in the form of a suspension in vaseline oil.

which it was poured on ice. The separated product (b) was recrystallized to a constant melting point (Table 2).

Reaction of 2-phenylamino-4-methylthiazole with propionic anhydride. 1) Without addends. 0.5 g of 2-phenylamino-4-methylthiazole and 2.5 ml of propionic anhydride were refluxed for two hours, after which the flask contents were poured on ice. The separated 2-propionylphenylamino-4-methylthiazole was recrystallized from dilute (1:2) propionic acid. It formed plates with m. p. 101-103°. Yield: 0.58 g (89.6%).

Found %: N 11.26. $C_{13}H_{14}ON_2S$. Calculated %: N 11.38.

2) In the presence of concentrated sulfuric acid. 0.5 g of 2-phenylamino-4-methylthiazole, 2.5 ml of propionic anhydride and 3 drops of concentrated sulfuric acid were refluxed for three hours, after which the solution was poured on ice. The separated 3-propionyl-4-methyl-2-phenylimino-4-thiazoline was recrystallized from alcohol. Rectangular prisms with m.p. 164-166°. Yield: 0.5 g (77.3%).

Found %: N 11.01. $C_{13}H_{14}ON_2S$. Calculated %: N 11.38.

3-p-Chlorophenyl-4-methyl-2-imino-4-thiazoline. 1.86 g of p-chlorophenylthiourea, 0.92 g of chloroacetone, 5 ml of alcohol and 1 ml of concentrated hydrochloric acid were refluxed on a steam bath for 45 minutes. A precipitate of 3-p-chlorophenyl-4-methyl-2-imino-4-thiazoline hydrochloride formed on cooling the solution. Yield: 2 g (77%).

Found %: N 10.79. $C_{10}H_9N_2ClS \cdot HCl$. Calculated %: N 10.72.

The base of 3-p-chlorophenyl-4-methyl-2-imino-4-thiazoline was obtained on neutralization of an aqueous solution of the hydrochloride with 30% sodium hydroxide solution. M.p. 113-114°. Yield: 1.3 g (58%).

3-p-Methoxyphenyl-4-methyl-2-imino-4-thiazoline was prepared similarly. Its hydrochloride formed prisms. Yield: 2.05 g (80%).

Found %: N 10.74. $C_{11}H_{12}ON_2S \cdot HCl$. Calculated %: N 10.91.

Free base: m.p. 144-145°. Yield: 1.4 g (64%).

Acetylation of 3-p-Chlorophenyl-4-methyl-2-imino-4-thiazoline with acetic anhydride. 1 g of 3-p-chlorophenyl-4-methyl-2-imino-4-thiazoline was dissolved in 3 ml of acetic anhydride at room temperature. After a 15 minute boiling, the solution was poured on ice. The resulting precipitate of compound (XI) was recrystallized to a constant melting point. It formed prisms with rhombic form (from alcohol); m.p. 172-172.5°. Yield: 0.81 g (68%).

Found %: N 10.72. $C_{12}H_{11}ON_2ClS$. Calculated %: N 10.51.

The acetyl compound (XII) was prepared similarly. Plates (from alcohol); m. p. 209-211°. Yield: 1 g (84%).

Found %: N 10.72. $C_{13}H_{14}O_2N_2S$ Calculated %: N 10.68.

TABLE 3

Sub-stance	λ_{max}	lg ε	λ_{min}	lg ε	λ_{max}	lg ε
(IX)	236	2.42	251	2.08	304	2.23
(X)	—	—	265	2.08	305	3.20
(XI)	220	3.23	265	2.17	305	3.16
(XII)	226	3.20	262	2.23	305	3.19

The ultraviolet absorption spectra of compounds (IX-XII) are given in Table 3.

SUMMARY

1. 2-Methyl- and 2-phenylaminothiazoles yield two isomeric acyl derivatives, which correspond to two tautomeric forms of 2-aminothiazole, in acylation under different conditions. The spectroscopic data indicate that the low-melting acetyl derivative is the amide (the acetyl group is at the amino group nitrogen atom), while the high-melting derivative is the imine — (the acetyl group is at the ring nitrogen atom).

2. It was established that the similarly constituted heterocyclic compounds capable of tautomerism (derivatives of 2-aminothiodiazole, 2-aminopyridine, etc.) yield only one acetyl derivative under these conditions.

3. It was shown that the low-melting acyl derivatives are transformed into the high-melting isomers in the presence of acid anhydrides (acetic, propionic) and concentrated sulfuric acid.

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SYNTHESIS OF ORGANOPHOSPHORUS COMPOUNDS FROM HYDROCARBONS AND THEIR DERIVATIVES

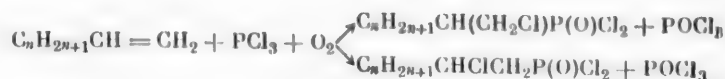## IX. OXIDATIVE CHLOROPHOSPHONATION OF 1-BUTENE, 2-BUTENE, AND CYCLOHEXENE

Yu. M. Zinov'ev and L. Z. Soborovskii

It was pointed out in the first communication about the reaction of hydrocarbons, phosphorus trichloride and oxygen that 1-butene yields in this reaction a chloride of chlorobutylphosphonic acid [1]. The structure of this compound was not considered at that time.
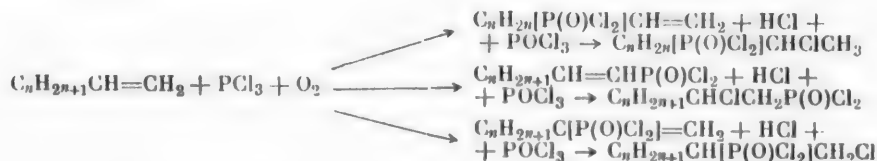
It was shown in the present work that the chlorobutylphosphonic dichloride formed from 1-butene is a mixture of isomeric compounds. Fractions, which did not differ in composition, but which possessed different boiling points, were isolated after a distillation of relatively large amounts of the indicated substance (500 g) Oxidative chlorophosphonation of 2-butene led to the isolation of a chlorobutylphosphonic dichloride which boiled within a relatively narrow interval. The constants and the composition of the isolated fractions are compared in the table. There, we also give for comparison the chlorides of isomeric chlorobutylphosphonic acids obtained by oxidative chlorophosphonation of 1- and 2-chlorobutanes.

The cause of the origin of isomeric compounds during the oxidative chlorophosphonation of olefins may lie in the following reactions.

1) Saturation of the ethylenic bond as a result of addition of the chlorine atom and the $POCl_2$ residue, which may occur in two directions.

$$C_nH_{2n+1}CH = CH_2 + PCl_3 + O_2 \left\langle \begin{array}{l} C_nH_{2n+1}CH(CH_2Cl)P(O)Cl_2 + POCl_3 \\ C_nH_{2n+1}CHClCH_2P(O)Cl_2 + POCl_3 \end{array} \right.$$

2) Substitution of one of the hydrogen atoms by the $POCl_2$ residue and a subsequent addition of the resulting hydrogen chloride to the double bond.

$$C_nH_{2n+1}CH{=}CH_2 + PCl_3 + O_2 \begin{array}{l} C_nH_{2n}[P(O)Cl_2]CH{=}CH_2 + HCl + \\ + POCl_3 \rightarrow C_nH_{2n}[P(O)Cl_2]CHClCH_3 \\ C_nH_{2n+1}CH{=}CHP(O)Cl_2 + HCl + \\ + POCl_3 \rightarrow C_nH_{2n+1}CHClCH_2P(O)Cl_2 \\ C_nH_{2n+1}C[P(O)Cl_2]{=}CH_2 + HCl + \\ + POCl_3 \rightarrow C_nH_{2n+1}CH[P(O)Cl_2]CH_2Cl \end{array}$$

The course of the reaction according to the second scheme, according to which the double bond is initially preserved in the molecule, is more probable since many examples are known of the entry of unsaturated compounds into substitution reactions [3].

The boiling point of one of the fractions of chlorobutylphosphonic dichloride prepared from 1-butene and shown in the table, coincides with the boiling point of the substance formed from 2-butene. It is known that the introduction of the $POCl_2$ residue into the methyl group during the oxidative chlorophosphonation of paraffins occurs with more difficulty than the introduction of it into the methylene group [2]. Since 2-butene does not

No. of substance	Starting substance	The synthesized chloride	B. p. (pressure in mm)	d	n_D^{20}	MR_D found	MR_D calc.	Location of Cl : $POCl_2$ substit.	% Isomer relative to the total chloride obtained
1	1-Butene	$CH_3CH_2CHClCH_2POCl_2$	85—86° (2)	1.3925	1.4925	43.6	43.59	2:1, 1:2	26.8
2		$CH_3CH_2CH(CH_2Cl)POCl_2$	73—74 (2)	1.3950	1.4857	43.0	43.59	2:3	73.2
3		$CH_3CHClCH(CH_3)POCl_2$							
4	2-Butene	$CH_3CHClCH(CH_3)POCl_3$	70—74 (2)	1.3831	1.4820	43.13	43.59	2:3	100
5	1-Chlorobutane	$CH_3CH_2CH_2CHClPOCl_2$	78—79 (2)	1.3779	1.4886	43.84	43.59	1:1	9.5
6		$CH_3CH_2CH(CH_2Cl)POCl_2$	84—85 (2)	1.3948	1.4946	43.68	43.59	1:2	20.5
7		$CH_3CHP(O)Cl_2]CH_2CH_2Cl$	95—98 (2)	1.4028	1.4963	43.57	43.59	1:3	54.0
8		$CH_2ClCH_2CH_2POCl_2$	110—113 (2)	1.3952	1.4950	43.77	43.59	1:4	16.0
9	2-Chlorobutane	$C_4H_8ClPOCl_2$ ••	85—93 (2.5)	1.3903	1.4905	43.57	43.59	2:1—4	—
10	Cyclohexene	$C_6H_{10}ClPOCl_2$ •••	127—130 (3)	1.4162	1.5287	51.13	50.63	—	—
11		$C_6H_{10}POCl_2$	99—102 (2)	1.3520	1.5250	45.09	45.29	—	—

• Described earlier [2].
•• Mixture of isomers.
••• Substance 10 was contaminated by substance 11.

have a methylene group; the course of the reaction for this compound according to scheme 2 is less probable.

Therefore, both compounds hould be assigned the structure of 2-chlorobutyl-3-phosphonic dichloride. This compound may arise from the oxidative chlorophosphonation of 1-butene only as the result of reactions which proceed according to scheme 2. The other fraction, evidently, is a mixture of 2-chloro-1-phosphonic and 1-chloro-2-phosphonic dichlorides formed according to scheme 1. The properties of this fraction are close to the properties of the substance prepared from 1-chlorobutane (see table, compound 6).

As it is clear from the data in the table, the predominant reaction is that following scheme 2. An indirect confirmation of the correctness of the above considerations about the course of oxidative chlorophosphonation of 1-butene is the formation of a small amount of butyl chloride which was isolated from the reaction mixture. The formation of this compound is explained by the addition of hydrogen chloride, which forms in the oxidative chlorophosphonation, (in case the reaction proceeds by scheme 2) to butylene which is present in the solution (the reaction was run at temperatures which were below the boiling point of 1-butene).

A mixture of chlorocyclohexyl- and cyclohexenylphosphonic dichlorides was isolated after the oxidative chlorophosphonation of cyclohexene. * It was impossible to isolate the indicated chlorides in the pure state by fractionation of the reaction mixture. The lower fraction, in which the cyclohexenylphosphonic dichloride should have been present, contained much unhydrolyzable chlorine and was evidently, a mixture of both substances. In order to prepare cyclohexenylphosphonic dichloride in the pure state, we heated the low-boiling part of the reaction mixture with activated carbon — an agent which facilitates the cleavage of hydrogen halides [5] — in order to cleave hydrogen chloride from it. After this treatment, we succeeded in distilling, without any difficulties, the substance which turned out to be cyclohexenylphosphonic dichloride. Evidently, chlorocyclohexylphosphonic dichloride is formed in the oxidative chlorophosphonation of cyclohexene; part of this product loses hydrogen

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*Isbell and Wadsworth assert erroneously that it is impossible to isolate any definite compounds from the reaction products of cyclohexene, phosphorus trichloride and oxygen [4].

chloride during the distillation, being transformed into cyclohexenylphosphonic dichloride.

EXPERIMENTAL

1. <u>Oxidative chlorophosphonation of 1-butene.</u> a) A mixture of equal volumes of 1-butene and oxygen was passed through phosphorus trichloride until the reaction ceased. The following fraction was isolated from the reaction mixture:

B. p. 80-86° at 3.5 mm, d^{20}_4 1.4010, n^{20}D 1.4930, MR_D 43.4; calc. 43.59.
Found %: C 23.11, 23.00; H 4.08, 3.90; P 15.48, 15.28. $C_4H_8OCl_3P$. Calculated %: C 22.92, H 3.85; P 14.79.

The following fractions were obtained from 75.7 g of the resulting substance after a redistillation under vacuum (2 mm): 1st 60-75°, 2.4 g; 2nd 73.74°, 31.5 g; 3rd 75-85°, 3.9 g; 4th 85-86°, 10.8 g. Residue: 4.8 g; 9.0 g condensed in a trap chilled with carbon dioxide snow.

2nd fraction. Found %: C 23.01, 22.93; H 4.99, 4.70. MR_D 43.0.

4th fraction. Found %: C 23.06, 22.88; H 3.71, 4.0. MR_D 43.6

b) Oxygen was passed through a mixture of 1-butene (41.0 g) and phosphorus trichloride (236.0 g) at −30° until the reaction ceased. A fraction with b. p. 85-100° at 5 mm (43.0 g, 28.1%) was isolated from the reaction mixture. After redistillation, we isolated the fractions: b. p. 72.76° at 2 mm, 19.1 g, and 80.83° at 2 mm, 5.1 g, similar to those formed in experiment a).

2.7 g of a light oil was isolated from the low boiling products boiling below 105° as a result of treating this with water; this oil yielded fractions with b. p. 68-70° and 78-80°. For 2-chlorobutane: b. p. 67-68° [6]; for 1-chlorobutane: 78° [7].

2. <u>Oxidative chlorophosphonation of 2-butene.</u> 59.0 g (31.2%) of the following substance was isolated from 307 g of phosphorus trichloride and 83 g of 2-butene under conditions of experiment 1b :

B. p. 72-75° at 2.5 mm, d^{20}_4 1.3831, n^{20}D 1.4820, MR_D 43.13; calc. 43.59.
Found %: C 23.85, 23.60; H 4.90, 4.19. $C_4H_8OCl_3P$. Calculated %: C 22.92; H 3.85.

3. <u>Oxidative chlorophosphonation of 1-chlorobutane.</u> Oxygen was passed at 20° into the mixture of 20.5 g of 1-chlorobutane and 137.5 g of phosphorus trichloride until the reaction ceased. A fraction with b. p. 75-120° at 2 mm was isolated. Yield: 21.9 g (47.2%).

150 g of the substance (from several experiments) was fractionated at 2 mm. The following fractions were isolated: 1st 73-78°, 3.5 g; 2nd 78-79°, 10.5 g; 3rd 79-84.5°, 2.2 g; 4th 84.5-85.5°, 21.4 g; 5th 85.5-95°, 7.5 g; 6th 95-98°, 62.8 g; 7th 98-110°, 5.6 g; 8th 110-113°, 12.0 g. Residue: 18.6 g.

2nd fraction. d^{20}_4 1.3779, n^{20}D 1.4886, MR_D 43.84.
Found %: C 22.15; 22.60; H 3.72, 4.00; Cl (hydrolyzable) 34.36, 34.21.
4th fraction. d^{20}_4 1.3948, n^{20}D 1.4946, MR_D 43.68.
Found %: C 23.40, 23.04; H 3.93; Cl (total content) 50.84, 50.49; Cl (hydrolyzable) 33.25, 33.50; P 14.67, 15.31.
6th fraction. d^{20}_4 1.4028, n^{20}D 1.4963, MR_D 43.57.
Found %: C 23.73, 23.86; H 4.37, 4.67; Cl 50.49, 50.81; Cl (hydrolyzable) 33.50, 33.70; P 14.86, 15.45.
8th fraction. d^{20}_4 1.3952, n^{20}D 1.4950, MR_D 43.77.
Found %: C 22.04, 22.32; H 3.78, 3.84; Cl 51.35, 51.29; Cl (hydrolyzable) 33.64, 33.64; P 14.79. $C_4H_8OCl_3P$. Calculated %: C 22.92; H 3.85; Cl 50.80 (hydrolyzable) 33.86; P 14.79. MR_D 43.59.

4. <u>Oxidative chlorophosphonation of 2-chlorobutane.</u> Oxygen was passed through a mixture of 11.0 g of 2-chlorobutane and 138 g of phosphorus trichloride until the reaction ceased. 8.0 g of a substance with b. p. 85-93° at 2.5 mm, which is rapidly hydrolyzed by water, was isolated. Yield: 35.4%.

d^{20}_4 1.3903, n^{20}D 1.4505, MR_D 43.57; calc. 43.59.
Found %: Cl (hydrolyzable) 33.60, 33.61. $C_4H_8OCl_3P$. Calculated %: Cl (hydrolyzable) 33.85.

5. Oxidative chlorophosphonation of cyclohexene. a) Oxygen was passed through the mixture of 41.0 g of cyclohexene and 455 g of phosphorus trichloride at 20° until the reaction ceased. A substance with b. p. $120-135^\circ$ at 5 mm was isolated; yield: 47.7 g (40.4%). The following fractions were isolated on redistillation (at 4 mm): 1st $110-118^\circ$, 1.2 g; 2nd $118-124^\circ$, 20.0 g; 3rd $123-135^\circ$, 21.0 g, d_4^{20} 1.4227, n_D^{20} 1.5288. All fractions decolorized the aqueous potassium permanganate solution.

A substance with b. p. $127-130^\circ$ at 3 mm was isolated from the third fraction.

d_4^{20} 1.4162, n_D^{20} 1.5287. MR_D 51.13; calc. 50.63.
Found %: C 32.24, 31.93; H 4.49, 4.51; Cl 45.9. $C_6H_{10}OCl_3P$. Calculated %: C 30.59; H 4.28; Cl 45.34.

2nd fraction: d_4^{20} 1.3896, n_D^{20} 1.5280, MR_D 52.5; calc. 50.63.
Found %: Cl (hydrolyzable) 34.8; Cl 40.7. $C_6H_{10}OCl_3P$. Calculated %: Cl (hydrolyzable) 30.11; Cl 45.34.

b) 10.0 g of the second fraction was heated in a distillation flask under vacuum with 3 g of activated carbon previously dried at 100° under vacuum. 6.5 g of a colorless substance distilled at $155-170^\circ$ (20-30 mm), the redistillation of which yielded the substance with b.p. $99-102^\circ$ at 2 mm.

d_4^{20} 1.3520, n_D^{20} 1.5250, MR_D 45.09; calc. 45.29.
Found %: C 36.89, 36.16; H 4.45, 4.84; Cl 36.70. $C_6H_9OCl_2P$. Calculated %: C 36.20; H 4.45; Cl 35.63.

SUMMARY

1. Oxidative chlorophosphonation of olefins containing methylene groups proceeds in two directions, one of which is the addition of chlorine atoms and $POCl_2$ residues to the double bond, the other direction being the substitution of hydrogen by the phosphorus-containing group.

2. Oxidative chlorophosphonation of 1-butene, 2-butene and cyclohexene was accomplished.

3. Isomeric chlorobutylphosphonic dichlorides and cyclohexenylphosphonic and chlorocyclohexylphosphonic dichlorides were synthesized.

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CONCERNING THE ACYLATION OF CUPRIACETOACETIC ESTER

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In continuation of the previously reported study [1], we studied the effect of the character of the active reagent on the direction of the substitution reaction (at O or at C) in the example of acylation of cupriaceto-acetic ester. Acetyl fluoride, acetic anhydride and trichloroacetyl chloride were taken as the acylating agents.

While for the silver derivatives of a keto-enol system (and the related systems) a greater tendency toward the formation of O-substituted reaction products has been evidently always noted relative to the corresponding derivatives of the alkali metals in reactions with alkyl or acyl halides, the dependence for the copper enolates turned out to be more complex [1, 2-4]. Thus, cupriacetoacetic ester is acylated by acetyl chloride and ben-zoyl chloride at the O-atom [5, 6] while sodioacetoacetic ester yields mainly the C-derivatives with the same reagents. The relations are reversed with chlorocarbonic ester [7], with chloromethyl ether [8] and with phos-gene [9].

The experimental data on alkylation and acylation of copper derivatives of acetoacetic ester are mainly limited to the above-mentioned examples. No systematic studies had been made. This urged us to add to the existing experimental data.

As it was found, acetyl fluoride, acetic anhydride and trichloroacetyl chloride react with cupriacetoacetic ester at the carbon atom (see table).

For the example of acylation with acetyl fluoride and acetic anhydride it was established that the de-liberately introduced enol acetate of acetoacetic ester is recovered from the reaction mixture unchanged in yields of 78-90% (table, exp. 2, 4 and 7). Therefore, it is possible to consider that α-acetylacetoacetic ester is formed as the result of the primary substitution reaction and not as the result of a secondary process of isom-erization of the enol acetate.*

A change of the duration of the reaction (see table, experiments with acetyl fluoride), the amount and the character of the solvent (see table, experiments with acetyl fluoride and acetic anhydride) do not reflect themselves in the direction of the substitution.

Since the literature lacks any data on the reaction of sodioacetoacetic ester with acetyl fluoride and with trichloroacetyl chloride, we also ran these reactions. Acetyl fluoride and sodium enolate yielded the α-acetylacetoacetic ester (table, expt. 11). As the result of acylation of the sodium enolate with trichloro-acetyl chloride we isolated bis-trichloroacetylacetoacetic ester (I) in 40% yield along with α-trichloroacetyl-acetoacetic ester (II) identified through its copper derivative (III).

The resulting data indicate that acetyl fluoride, acetic anhydride and trichloroacetyl chloride behave in the reaction with cupriacetoacetic ester like chlorocarbonic ester and chloromethyl ether and differ sharply

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*In the previous studies for the establishment of the presence or the absence of this form of isomerization only the action of the starting materials was tested [10, 11], while the intermediate and final reaction pro-ducts might be the active isomerizing agents, as well as a combination of various factors which are manifested under the reaction conditions.

from the behavior of acetyl chloride (the reaction of acetyl chloride was run by us for comparison purposes in chloroform; table, expt. 12).

In the course of this work it was necessary for us to find the most convenient method of determination of the amount of α-acetylacetoacetic ester in a mixture with the unreacted acetoacetic ester. It is known that α-acetylacetoacetic ester may be separated from acetoacetic ester by dissolution in sodium carbonate [7] or by precipitation in the form of the copper derivative in acetic acid medium [12].

Acylation of Cu and Na Enolates of Acetoacetic Ester

Expt. no.	Enolate	Amount (in moles)	Acylating agent	Amount (in moles)	Am't of enol acetate (in g)	Solvent (in ml)		Temperature	Time (in hours)	Yield of the derivative (in %)	
										c	0
1		0.037		0.055	--	CHCl$_3$	20	20°	48	59.7	—
2		0.037		0.055	10.75		20	20	48	60.5	80.0
3		0.037	CH$_3$COF	0.055	--		30	20	48	65.7	—
						Ligroine	20				
4		0.065		0.055	21.4		30	20	264	65.7	78.0
5	Copper	0.110		0.077	---		30	20	216	93.3	—
6		0.050		0.10	—	CHCl$_3$	25	55-60	45	70.0	—
7		0.050	(CH$_3$CO)$_2$O	0.10	13.73		25	55-60	45	70.2	90.4
8		0.050		0.10	--		40	55-60	45	73.7	—
9		0.031		0.318	..	(CH$_3$CO)$_2$O		55-60	45	64.2	—
10		0.10	Cl$_3$CCOCl	0.214	--	Ether 150		20	48	71.3	—
11	Sodium	0.10	CH$_3$COF	0.109	---	Ether 75		0	3.5	90.0	Traces
12	Copper	0.037	CH$_3$COCl	0.051	—	Chloroform	20	20	24	—	5.84 g

Note: Experiments 2 and 3 were run like experiment 1, while experiments 7-9 similarly to experiment 6. In experiment 5 the reaction mixture was diluted with ether and was shaken with cooling with dilute hydrochloric acid, after which the C-derivative was isolated in the usual manner. In experiment 11 the acetyl fluoride was gradually added to the enolate. In experiment 12 the chloride was added rapidly to the enolate.
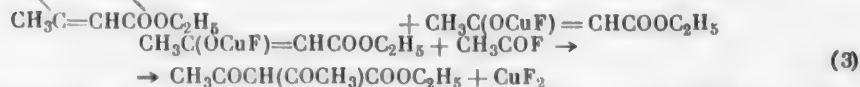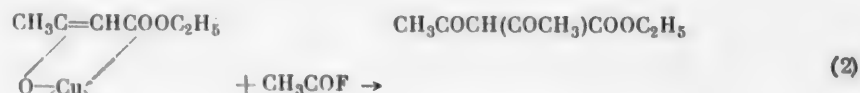
We used the refractometric method. By measurement of the indexes of refraction of authentically prepared mixtures of α-acetylacetoacetic ester and acetoacetic ester, we established that a linear dependence exists between the index of refraction of the mixture and the weight percent content of the components in it. This permitted us to calculate with an accuracy sufficient for our purposes ($\pm$ 2%) the content of the α-acetylacetoacetic ester in this mixture by the usual formula ([1]):

$$A = \frac{n^{20}D \text{ (of mixture} - n^{20}D \text{ (acetoacetic ester)}}{n^{20}D \text{ (acetylacetoacetic ester)} - n^{20}D \text{ (acetoacetic ester)}}$$

In all probability the change in the index of refraction of the mixture connected with the displacement of the keto-enol equilibrium of acetoacetic ester is not so great as to affect the measurements at the indicated degree of accuracy.

It was discovered simultaneously that another interesting phenomenon existed. A mixture of acetoacetic ester and its α-acetyl derivative, in contrast to pure acetoacetic ester, does not change its index of refraction after a distillation. Evidently α-acetylacetoacetic ester, as a rather acid enol, aids the rapid establishment of the keto-enol equilibrium of the acetoacetic ester.

Acylation (at O) of cupriacetoacetic ester by acetyl chloride is accompanied by formation of α-chloro-acetoacetic ester and cuprous chloride [6]. The reaction proceeds differently with acetyl fluoride: cuprous fluoride and fluoroacetoacetic ester are not formed. The reaction of acetyl fluoride with cupriacetoacetic ester may be shown by the following equations.

$$CH_3C=CHCOOC_2H_5 \qquad\qquad CH_3COCH(COCH_3)COOC_2H_5$$

$$O-Cu \qquad\qquad + CH_3COF \rightarrow \tag{2}$$
$$O$$
$$CH_3C=CHCOOC_2H_5 \qquad\qquad + CH_3C(OCuF)=CHCOOC_2H_5$$

$$CH_3C(OCuF)=CHCOOC_2H_5 + CH_3COF \rightarrow$$
$$\rightarrow CH_3COCH(COCH_3)COOC_2H_5 + CuF_2 \tag{3}$$

It was discovered previously [13] that acetic anhydride is capable of acylating (at C) the free acetoacetic ester in the presence of small amounts of cupriacetoacetic ester. In this connection, it is as yet difficult to assert how the reaction of cupriacetoacetic ester with acetic anhydride proceeds in our case: whether the acylation of the copper enolate directly or that of the free acetoacetic ester takes place. The latter substance may form from the copper enolate by the action of traces of acetic acid or (during the course of the reaction) that of α-acetylacetoacetic ester.

The reaction of acetyl fluoride or trichloroacetyl chloride with free acetoacetic ester is not catalyzed by cupriacetoacetic ester, as shown by separate experiments.

The tendency of acetyl fluoride and trichloroacetyl chloride to react at the C-atom of cupriacetoacetic ester may be explained on the basis of general considerations about the effect of the character of the acting reagent on the direction of the substitution reaction of metallic derivatives of tautomeric systems [14].

EXPERIMENTAL

Acetoacetic ester. B. p. 103° at 55 mm; for freshly distilled sample: $n^{20}D$ 1.4250. After standing: $n^{20}D$ 1.4200 (does not change).

Enol acetate of acetoacetic ester. Prepared by acylation of acetoacetic ester in the presence of pyridine [15]. B. p. 98° at 16 mm, $n^{20}D$ 1.4450.

Cupriacetoacetic ester. [16]. Recrystallized from toluene. M. p. 186° (with decomposition).

Acetyl fluoride. Prepared without admixtures of the chloride by the reaction of acetic anhydride with potassium fluoride [17]; b. p. 20-22°.

Reaction of acetyl fluoride with cupriacetoacetic ester. Experiment 1. 12.0 g of cupriacetoacetic ester, 3.42 g of acetyl fluoride and 20 ml of dry chloroform were placed in an ampule. A noticeable part of the enolate passed into solution during this operation. After a three-hour shaking the ampul was set aside for 45 hours. The reaction mixture was a blue solution with a small amount of a white precipitate; this was diluted with 100 ml of dry ether. The whole was shaken energetically with 25 ml of sodium carbonate solution, saturated at 0°, in the presence of ice, then with 125 ml of 10% sodium hydroxide solution, cooled externally with a snow-salt mixture. The resulting copper-containing precipitate was separated by centrifuging. The ethereal layer was washed several times with ice water and dried over sodium sulfate.

No residue, and consequently no enol acetate of acetoacetic ester, was found after the distillation of the solvent from the ethereal solution. The aqueous alkaline solution was combined with the precipitate. 150 ml of ether was added to the resulting suspension, after which hydrochloric acid (1:1) was added with ice cooling and shaking until strongly acid (to Congo red). The etheral solution was separated, washed with water and dried with sodium sulfate. The solvent was distilled off under a slight vacuum and the residue was distilled under reduced pressure. After a small fore-run, the following fractions were collected: 1st, b.p. 80-93° at 16 mm, $n^{20}D$ 1.4417, 3 g; 2nd, b. p. 93-96° at 16 mm, $n^{20}D$ 1.4686, 4686, 4.8 g; the first fraction — a mixture of acetoacetic ester and α-acetylacetoacetic ester; the second fraction consisted mainly of α-acetylaceto-acetic ester. For the pure substance: b. p. 96° at 16 mm, $n^{20}D$ 1.4725. Literature data: b. p. 104° at 18 mm [18] 97-98° at 15 mm [19], $n^{20}D$ 1.4729 [19].

It was found by means of formula (1) that the first fraction contained 1.24 g, and the second fraction — 4.44 g of α-acetylacetoacetic ester. Total yield: 5.68 g (59.7% based on acetyl fluoride taken). The copper derivative of α-acetylacetoacetic ester, m. p. 151° (from benzene + petroleum ether); according to [12]: m.p. 151°.

Experiment 2. 12.0 g of cupriacetoacetic ester, 3.42 g of acetyl fluoride, 10.75 g of acetoacetic ester enol acetate and 20 ml of chloroform was placed into an ampul. The reaction conditions and treatment were exactly the same as in experiment 1. 8.6 g (80% of the amount taken) of the enol acetate was recovered from the reaction; b. p. 98° at 16 mm, n_D^{20} 1.4450.

Fractions of acidic character were isolated: 1st, b. p. 80-93° at 16 mm, n_D^{20} 1.4340, 3.4 g; 2nd, b. p. 93-97° at 16 mm, n_D^{20} 1.4680, 5.3 g. It was calculated by formula (1) that the total yield of α-acetylacetoacetic ester was 5.74 g (60.5%).

Note. During the usual work-up of the mixture of 10 g of acetoacetic ester, 2.5 ml of acetyl fluoride and 20 ml of chloroform, no α-acetylacetoacetic ester was formed.

Reaction of acetic anhydride with cupriacetoacetic ester. For all experiments with acetic anhydride the ampuls were previously treated with boiling concentrated hydrochloric acid [13] for 3-4 hours and were then dried.

Experiment 6. The ampul containing 16.1 g of cupriacetoacetic ester, 10.23 g of acetic anhydride, and 25 ml of chloroform was heated on a water bath for 45 hours at 55-60°. The reaction mixture — a blue solution with a precipitate — was diluted with 150 ml of ether and was acidified with hydrochloric acid (1 : 2), cooled with ice-salt mixture, to a definitely acid reaction (disappearance of blue color in the ethereal layer). The ethereal solution was separated, washed with ice water and extracted successively with 80 ml of sodium carbonate solution and 200 ml of 10% sodium hydroxide with internal cooling by means of ice. The ethereal layer was dried with sodium sulfate; the solvent was distilled off. No residue remained. Products of acidic character were isolated in the usual manner from the combined aqueous solutions. The following fractions were collected: 1st, b.p. 82-84° at 8 mm, n_D^{20} 1.4640, 1.66 g; 2nd, b. p. 84-85° at 8 mm, n_D^{20} 1.4700, 11.2 g. The total content of α-acetylacetoacetic ester, calculated by formula (1), was 12.06 g (70.0%). The boiling point of pure α-acetylacetoacetic ester is 85° at 8 mm, n_D^{20} 1.4725.

Notes: 1. As a result of heating (60°, 5 days) 13 g of acetoacetic ester, 10.2 g of acetic anhydride and 25 ml of chloroform in an ampul pretreated with hydrochloric acid, no α-acetylacetoacetic ester was formed (test of the distilled acidic fraction with copper acetate in acetic acid medium).

2. A mixture of 13 g of acetoacetic ester and 10.2 g of acetic anhydride was diluted with 50 ml of ether and treated as usual. No acylation of acetoacetic ester occurred (test for α-acetylacetoacetic ester with copper acetate).

3. 10.0 g of acetoacetic ester, 21.6 g of acetic anhydride and 1 g of cupriacetoacetic ester were heated for four days on a steam bath, the acetic anhydride was distilled off under vacuum from a water bath, and α-acetylacetoacetic ester was extracted with sodium carbonate from the residue, the product being isolated later by the usual means; yield: 10.1 g (64.8%).

Reaction of trichloroacetyl chloride with cupriacetoacetic ester. 36.4 g of trichloroacetyl chloride was gradually added with stirring and ice cooling to 32.18 g of cupriacetoacetic ester in 150 ml of dry ether. The reaction mixture was stirred for about three hours longer with cooling and was set aside for 48 hours. The precipitate of the copper salts was separated by centrifuging and was washed with dry ether. Ether was distilled from the combined solutions under a slight vacuum. The residue was filtered and vacuum distilled. The following fractions were collected: 1st up to 111° at 5.5 mm, 6.01 g; 2nd 111-116° at 5.5 mm, 39.28 g. The second fraction was α-acetylacetoacetic ester (II); yield 71.3%.

B. p. 136° at 13 mm, 120° at 7 mm, 101.5° at 3 mm, n_D^{20} 1.4932.
Found %: C 34.89; H 3.38. $C_8H_9O_4Cl_3$. Calculated %: C 34.87; H 3.29.

(II) readily dissolves in dilute alkalies and gives a deep red color with ferric chloride. 3.0 g (91.5%) of the copper derivative (III) with m. p. 171.5° (with decomposition; from alcohol) — a blue finely crystalline powder — was obtained from 2.95 g of (II) dissolved in 20 ml of ether, by shaking with a saturated solution of copper acetate.

Note. In running the reaction of 18.2 g of trichloroacetyl chloride with 13.1 g of acetoacetic ester and 1 g of cupriacetoacetic ester in 75 ml of ether (left for 7 days at 20°) we isolated 1.16 g of (II) with b. p. 124° at 7.5 mm.

Reaction of trichloroacetyl chloride with sodioacetoacetic ester. 36.4 g of trichloroacetyl chloride was added gradually with stirring and ice cooling to sodioacetoacetic ester, prepared from 4.6 g of sodium and 28.0 g of acetoacetic ester in 150 ml of dry ether. After 48 hours the filtrate was distilled (reaction temperature about 20°). The following fractions were collected: 1st 52-100° at 5 mm, 13.8 g; 2nd 100-177° at 5 mm, 16.0 g; 3rd 177-182° at 5 mm, $n^{20}D$ 1.5034, 1671 g.

The third fraction was bis-(trichloroacetyl)acetoacetic ester (I); yield: 39.7%.

B. p. 161° at 3 mm, $n^{20}D$ 1.5045.
Found %: C 29.44; H 2.22. $C_{10}H_8O_5Cl_6$. Calculated %: C 28.53; H 1.92

(I) was insoluble in alkalies, did not give color with ferric chloride, and yielded trichloroacetamide with a concentrated ammonia solution. The second fraction was partly soluble in alkalies and gave (III) with copper acetate.

SUMMARY

The acylation of cupriacetoacetic ester with acetyl fluoride, acetic anhydride and trichloroacetyl chloride was studied. In all cases, the substitution occurred at the C-carbon atom of acetoacetic ester.

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INVESTIGATION OF THE PATHS OF HYDROGEN TRANSLOCATION DURING OXIDATION–REDUCTION REACTIONS

XII. THE REDUCTION OF TRIPHENYLCARBINOL

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The reduction of triphenylcarbinol by alcohols and formic acid is an example of an oxidation–reduction process involving disproportionation, and the sources and paths of the hydrogen can be easily established with the help of deuterium.

Alcohols reduce triphenylcarbinol to triphenylmethane in concentrated sulfuric acid at room temperature [1] or in presence of an excess of zinc chloride with application of heat [2]; formic acid reduces it on heating or on prolonged standing at room temperature [3-5].

Results of our earlier work [6] gave good grounds for suggesting that in both cases only hydrogen from the C–H groups of the reducing agents is transferred to the tertiary carbon atom of triphenylcarbinol during reduction of the latter, and that no hydrogen is donated by the hydroxyl groups of the carbinol itself or the reducing agents. It is also assumed that no protons are donated by the catalyst. The hypothesis has been advanced [7-9] that reduction of arylcarbinols by alcohols and formic acid goes through formation of the corresponding ethers or alcohols whose breakdown to triarylmethanes is accompanied by transfer of a proton of the catalyzing acid [8, 9].

It was of interest to obtain direct experimental evidence of the source of the hydrogen and of the path of its translocation during reactions of the above type, and to determine the magnitude of the kinetic isotope effect which would enable evaluation of certain characteristics of the transition state.

We investigated the reduction of triphenylcarbinol by methyl and ethyl alcohols in presence of zinc chloride, using the method of Kauffmann and Grombach [2]. In a first series of experiments, we examined alcohols labeled with deuterium in the hydroxyl group; in a second series, we investigated methyl-D alcohol CH_3DOH.

0.015 mole triphenylcarbinol was boiled with a 15-fold molar excess of methyl alcohol or a 10-fold excess of ethyl alcohol in presence of 0.14-0.15 mole anhydrous zinc chloride. In ethanol the reaction was completed in 1-1.5 hr; in methanol it was necessary to heat for 12-10 hour. After the reaction was completed and the reaction mixture had been cooled, the zinc chloride was dissolved with hydrochloric acid (1 : 5), the triphenylmethane was extracted with ether, and the ethereal extract was washed with water and dried. The ether was then driven off and the triphenylmethane recrystallized from ethanol. The yield was between 75 and 90% of the theoretical. M. p. 92-93°. The isotopic composition of the triphenylmethane was determined by the flotation method on the basis of the excess density of the water resulting from its combustion. Three parallel experiments were run with ethanol containing 20,590 γ of deuterium in the hydroxyl; the water from the combustion of the triphenylmethane from these experiments had an excess density of 16-19 γ. In four experiments with methanol (15,660 γ in the hydroxyl group) the water from the combustion of the isolated triphenylmethane had an excess density of 35-40 γ. This value exceeds the possible experimental error and is most probably due to the introduction into the triphenylmethane of a small quantity of deuterium by a secondary exchange reaction catalyzed by zinc chloride (similar to the aluminum chloride-catalyzed exchange [2]). There reduction

experiments with methanol labeled with deuterium in the methyl group gave heavy triphenylmethane. The water from combustion of the latter had an excess density of 223-260 γ, which corresponded to 3520-4100 γ of deuterium in the methyl group of triphenylmethane, since in the combustion of the triphenylmethane one atom of hydrogen entering into its molecule during reduction is diluted with 15 atoms of the hydrogen of the three benzene rings. The results show unequivocally that hydrogen from the C-H groups of the alcohols passes to the tertiary carbon atom of triphenylmethane during its reduction, but not hydrogen from their hydroxy groups or from the hydroxyl groups of the carbinol itself.

$$(C_6H_5)_3COH + RCD_2OH \xrightarrow{ZnCl_2} (C_6H_5)_3CD + RCDO.$$

Reduction experiments in methanol CH_2DOH enable calculation of the magnitude of the kinetic isotope effect during this reaction. Calculation was based on the formula $K_H/K_D = \dfrac{\ln(1-S)}{\ln\left(1-S\dfrac{x}{y}\right)}$ [22], where S is the degree of completion of the reaction, x and y are the contents of deuterium in the original alcohol and in the reaction product. Since reduction with methanol was performed in a 15-fold molar excess of reducing agent, only one-fifteenth of it could have been oxidized by the triphenylcarbinol; the degree of completion of the reaction therefore corresponded to $1/15 \times x = 6150$ γ; in three parallel experiments y was 3840, 4100 and 3520 γ. On the basis of these data, the mean value of $K_H/K_D = 1.6$.

In one of the experiments on reduction of triphenylcarbinol with methanol, heating of the reaction mixture was cut down by $\frac{1}{2}$ hour. In this case, the reaction product was nearly pure triphenylmethyl methyl ether, which was identified from its m.p. of 81-82° in a mixed melting test. The isotope composition of this product corresponded to the isotope composition of the original methyl-D alcohol CH_2DOH converted to $(C_6H_5)_3COCH_2D$

By further heating of the ether with methanol and $ZnCl_2$ for 12-10 hr the ether could be converted to triphenylmethane in good yield (80-90%). Heating for shorter periods of both the ether and the triphenylcarbinol led to formation of a mixture of products with m. p. from 57 to 70°. The components of this mixture could not be separated. The difficulty of separation indicated that the mixture consisted of triphenylmethane and triphenylmethyl methyl ether, since these two compounds have similar solubilities which are very different from the solubility of triphenylcarbinol.

On heating with methanol and $ZnCl_2$ the impure product was converted into pure triphenylmethane.

The results of these experiments leave no doubt that reduction with methyl alcohol leads to triphenylmethyl methyl ether, whose breakdown is accompanied by direct migration of hydrogen from the methyl groups of the alcohol to the tertiary carbon atom.

These results are at variance with the reaction mechanism whereby reduction goes by way of detachment by triphenylmethyl cations of hydride ions from the methyl groups of the alcohol, since carbonium ions must be formed with greater facility from the carbinol than from its ether.

It is impossible to account for the catalytic action of zinc chloride solely through its dehydrating ability, i.e., by catalysis of the formation of the ether; for according to Norris and Creswell [10] thermal decomposition of triphenylmethyl methyl ether ensues only at very much higher temperature (262°). On the other hand, the acidic catalysis of disproportionation of ethers of arylcarbinols is well-known [5, 7-9]. We can therefore advance the hypothesis that intramolecular migration of hydrogen in the ether is catalyzed by molecules of zinc chloride (Lewis acid or HCl formed by hydrolysis of the salt in water released during formation of the ether) or by some other acidic reagent formed in the reaction medium.

Since triphenylmethane can be obtained from triphenylmethyl methyl ether by heating with methanol and zinc chloride, i.e., in the absence of water, it is more likely that the decomposition is catalyzed by zinc chloride and not by HCl.

We do not yet have direct experimental evidence for the steps in the decomposition of the ether and in the attachment of hydrogen to the triphenyl methyl residue. In this connection the work of Balfe and co-workers [8] is significant. These workers showed that disproportionation of ethers of arylcarbinols in acid media can proceed in solvents like benzene, dioxane and acetone, but the reaction goes very much faster in presence

of alcohols; of the three possible schemes A, B and C, preference must therefore be given to C.
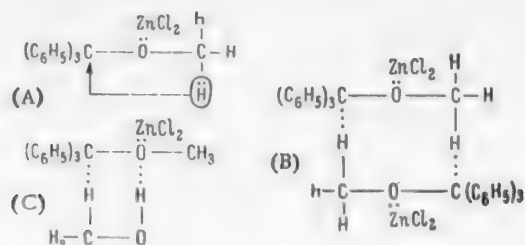
Addition of a zinc atom to the free electron pair of the ethereal oxygen causes a shift of the electrons and bond rearrangement, leading to formation of the reaction products. This interpretation of the reaction mechanism resembles that of the Meerwein-Pondorf reaction; in the latter the catalytic action of aluminum alcoholates is explained by the coordinative addition of an aluminum atom to the oxygen of the compound undergoing reduction [11].

The rate-determining step in the investigated reaction is the breakdown of the ether which is associated with migration of hydrogen. This follows both from our experiments on the reduction of triphenylcarbinol with methanol and from the fact that although the ethyl ether of triphenylcarbinol is formed more slowly than the methyl ether [12], the reduction with ethanol goes very much faster than with methanol. The isotope effect that we observed is in harmony with the foregoing facts. The low value of the isotope effect may be due either to the velocity of breakdown of the complex of ether with catalyst being of the same order as the velocity of its reformation, [13], or to synchronization of the rupture and formation of bonds in the transition complexes of the types of (A), (B) and (C). We consider the second explaination to be the more probable for the reason advanced in the preceding communication [14].

It is interesting to compare the results of our experiments with those of Bartlett and McCollum [17]. The latter paper was published after our investigations had been completed and had been reported in brief [16]. The authors in question studied the kinetics and mechanism of reduction of triphenylcarbinol and its substituted alcohols in sulfuric acid. With the help of deuterium it was demonstrated that hydrogen migrates in triphenylmethane from the α carbon atom of isopropyl alcohol with an isotope effect of 1.8.

Kinetic experiments, using spectrophotometry, showed that the reduction of triphenylcarbinol and of its ethyl ether are first order reactions. The authors were, therefore, unable to establish unequivocally which of the reaction components — the carbinol, its ether, sulfate or carbonium ion — was the active species in the reduction reaction. The low isotope effect found by the authors is close to the isotope effect in the $ZnCl_2$-catalyzed reduction with methyl alcohol. It would thus appear that the transition complexes leading to translocation of the hydrogen are similar in structure in both cases, i.e., that also in reduction in sulfuric acid the first reaction step is formation of the ether. The following considerations seem to us to make this hypothesis extremely probable. The existence of unsolvated carbonium ions is very improbable; on the other hand, the solvation of triphenylmethyl cations by molecules of solvent (alcohol) leads to formation of an ether, or rather of an acid conjugate with an ether.

$$(C_6H_5)_3\overset{+}{C} + (CH_3)_2CHOH \rightarrow (C_6H_5)_3\overset{+}{C}\text{-}\overset{\overset{H}{|}}{O}\text{--}CH(CH_3)_2$$
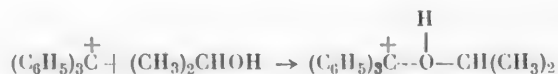
Since alcohols are associated liquids, not one but two molecules of alcohol may enter into the transition complex.
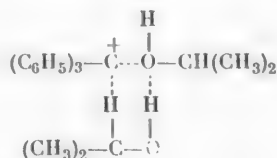
Evidence in support of such a structure of the transition complex is the negative entropy of activation found by Bartlett and McCollum which points to a considerable degree of order in the transition complex. The data of Balfe and co-workers [8] also favor such a structure.

Experiments on the reduction of triphenylcarbinol with formic acid HCOOD and DCOOH also showed that reduction of the carbinol goes at the expense of the hydrogen of the C-H bonds, and not of the O-H bonds of formic acid.

0.019 mole (5 g) carbinol was heated with 0.152 mole (7 g) 90% formic acid for 5-6 hour. After completion of the reaction and cooling of the reaction mixture, the resulting triphenylmethane was separated by filtration, washed with water, and crystallized from alcohol. The yield of product with m.p. 92-93° was 90-95%. The isotope composition of the triphenylmethane was determined in the same manner as in the reduction experiments with alcohols.

Four experiments using HCOOD containing 6500 γ of deuterium in the hydroxyl group gave triphenylmethane substantially free from deuterium. The water obtained by its combustion had an excess density of 6-17 γ.

Reduction with DCOOH containing 8130 γ of deuterium in the C-H grouping gave (in three experiments) triphenylmethane containing 4640, 4670 and 4780 γ of deuterium at the tertiary carbon atom.

We found the kinetic isotope effect from the isotopic composition of the original DCOOH and of the triphenylmethane formed, just as was done in the experiments with methanol. The value of S in this case was 1/8, since the reaction was carried out in an 8-fold molar excess of formic acid. The mean value of K_H/K_D found by this method was 1.8.

There are two views about the mechanism of reduction of triphenylcarbinol with formic acid. Bowden and co-workers [4] are of the opinion that reduction goes via formation of triphenylmethyl formate. They base this on the observation that triphenylmethyl formate already decomposes at 49° to form triphenylmethane and carbon dioxide.

Stewart [18] recently studied the kinetics of the reaction in dilute solutions of triphenylcarbinol and showed by spectrophotometry that the reaction mixture contains free carbonium ions and that the rate of reduction under the given conditions is proportional to the concentration of carbonium ions and formate anions. This author is inclined to favor the direct cleavage of hydride hydrogen from formate anions by carbonium ions, although the kinetic data are also in accord with intermediate formation of an ether. The reaction kinetics are rather complex; the velocity constant in particular is strongly dependent on the concentration of water in the system and reaches a maximum in 98% HCOOH. This demonstrates the important role of water in the process. It was responsible for the different values of the kinetic isotope effect found by Stewart in the reaction with 92% formic acid and with anhydrous acid. * The values of K_H/K_D were 2.5 and 4.9 respectively. In our experiments the formic acid contained even more water (10-12%); since the reaction was performed in considerably more concentrated carbinol solutions, an appreciable quantity of water separated during the reaction, and we obtained the still smaller value of 1.8 for K_H/K_D. The reduced kinetic isotope effect with increasing water concentration may be explained by the weaker solvating ability of formic acid (in comparison with water [19]) and by the fact that the hydrogen transfer step goes with participation not of free but of solvated carbonium ions. A sufficiently large quantity of water, which solvates carbonium and formate ions, may lead to formation of a transition complex (D) the migration of hydrogen in which is accompanied by a small isotope effect.

$$(C_6H_5)_3 \overset{+}{C} \cdots O-H$$
$$\vdots \qquad \vert$$
$$H \qquad H$$
$$\vert \qquad \vdots$$
$$O=C-O^-$$

(D)
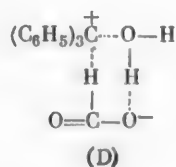
Such complexes are not formed in the absence of water. Reduction goes with detachment of hydrogen by carbonium ions. This process is accompanied by an isotope effect of normal magnitude comparable to the detachment of hydrogen by free radicals [20].

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*The work in question [18] was published in 1957 after our own experiments had been completed.

Syntheses of deuterated compounds. Methy-D alcohol CH_2DOH was prepared by the action of anhydrous benzoic acid, labeled with deuterium in the hydroxyl group, on an ethereal solution of diazomethane. 79 g benzoic acid was added gradually with cooling to an ethereal solution of diazomethane prepared from 100 g nitrosomethyl urea by Arndt's method [23]. After bubbles of nitrogen had ceased to come off, the ether was driven off and the methyl benzoate was distilled. The 195-202° fraction was collected. Hydrolysis of the methyl benzoate was effected with 17% sodium hydroxide solution, the mixture being heated so that methanol distilled off with progressive hydrolysis. Complete extraction of the deuterated methanol was facilitated toward the end of the reaction by addition to the flask of ordinary methanol which was then slowly distilled. The collected methyl alcohol was purified by fractionation. The yield of methanol with b. p. 65-66° was 72%, calculated on the methyl benzoate.

Formic acid-D HCOOD was prepared by exchange of pure anhydrous formic acid with D_2O and subsequent removal of the water by treatment with anhydrous oxalic acid, followed by cooling to 10 to −3° and collection of the deposited crystals. The resulting product was fractionated and the 101-101.5° cut was collected.

DCOOH was prepared from $Pb(OOCD)_2$ [15] by passage of H_2S through a heated porcelain tube filled with the solid lead formate. The formic acid that distilled off was condensed and purified by fractionation. It had a freezing point of +3° instead of 8.5° and d^{20} 1.207 instead of 1.220 for anhydrous HCOOH, corresponding to an acid with a water content of about 10%.

SUMMARY

1. Deuterium-labeled substances were employed for a study of the mechanism of reduction of triphenylcarbinol by formic acid as well as by methyl and ethyl alcohols in presence of zinc chloride.

2. It was shown that only hydrogen from the C−H groupings of the reducing agents enters into the resulting triphenylmethane when formic acid and alcohols are used as reducing agents.

3. The kinetic isotope effects on reduction of triphenylcarbinol by methyl-D alcohol CH_2DOH and by formic-D acid DCOH were found to be 1.6 and 1.8, respectively.

4. Data for the kinetic isotope effect were utilized for appraisal of the possible mechanisms of the investigated processes.

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DIALKYLAMINOALKYL ESTERS OF 3,4,5-TRIMETHOXYBENZOIC ACID

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In recent years a considerable number of alkaloids have been isolated from various species of Rauwolfia.
Some of these possess valuable pharmacological activity. The most important of these alkaloids is reserpine
(I), a highly active hypotesive and tranquilizing agent widely used in medicine.

It was recently reported that tranquilizing activity can be manifested by much simpler compounds contain-
ing only some of the structural elements characterizing reserpine. According to the literature the γ-diethyl-
aminopropyl ester of 3,4,5-trimethoxybenzoic acid (II) (n = 3, R' = R'' = C_2H_5) exhibits one-third of the activity
of reserpine. It has been suggested that the activity is associated with the similarity between the structure of
(II) (n = 3, R' = R'' = C_2H_5) and the structure of the part of reserpine corresponding to positions 2, 3, 4, 5, 6, 18,
19, 20 and 21 of the molecule of this compound [1].
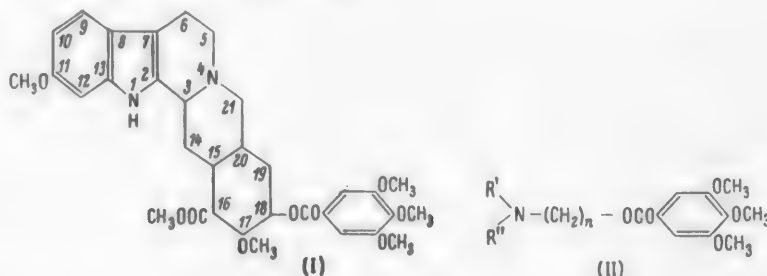
If this supposition were correct, we should be able to synthesize compounds of relatively simple structure
possessing reserpinelike tranquilizing and possibly also hypotensive activity.

On the basis of this reasoning, we prepared for pharmacological tests a series of twelve dialkylamino-
alkyl esters of 3,4,5-trimethoxybenzoic acid (II) with various lengths of carbon chain between the oxygen and
nitrogen atoms (n = 2, 3 or 4), and also with different substituents at the nitrogen atom (see table). In addition,
we prepared the corresponding ester of β-(N-methylpiperidyl)-carbinol (see the typical experiment in Experi-
mental). All of the esters, apart from (II) (n = 3, R' = R'' = C_2H_5) were synthesized by reaction of equimolar
quantities of 3,4,5-trimethoxybenzoyl chloride [2] with the appropriate aminoalcohol in a medium of benzene.
The ester bases were isolated in the analytically pure form in most cases even without fractionation in vacuo.
They were characterized in the form of the hydrochlorides and methiodides.

2-(N-Hexamethyleneimino)-ethanol-1, not described in the literature, as well as other aminoalcohols
with n = 2, were synthesized by reaction of hexamethyleneimine with ethylenebromohydrin. 4-Dialkylamino-
1-butanols were synthesized by reaction of 1 mole 1-acetoxy-4-bromobutane [3] with 2 moles of the appropriate
secondary amine (hexamethyleneimine, diethylamine, piperidine or morpholine) followed by acid hydrolysis
of the intermediately formed 1-acetoxy-4-dialkylaminobutanes (we did not isolate the latter in the pure state).
This method of preparation of 4-dialkylamino-1-butanols was simpler than other synthetic routes described in
the literature [4-7].

Dialkylaminoalkyl Esters of 3,4,5-Trimethoxybenzoic Acid

R'	R''	n	Base m. p.	Base b.p. (pressure in mm)	yield (%)	analysis for nitrogen (%) found	calc.	Hydrochloride m. p.	analysis for chlorine (%) found	calc.	Methiodide m. p.	analysis for iodine (%) found	calc.
CH_3	CH_3	2		180—181°(4)	72	4.91, 5.10	4.94	124.5—125.5	10.95, 10.99	11.13	175—176°	29.99, 30.06	29.94
C_2H_5	C_2H_5	2		175—180(1.5)	77.3	4.55, 4.60	4.50	156.5—157.0	10.13, 10.16	10.20	141—142	28.20, 28.23	27.99
—$(CH_2)_5$—		2	42—44°	[1]	88	4.39, 4.25	4.33	191.5—196.0	9.75, 9.75	9.85	167—168	27.42, 27.33	27.27
—$(CH_2)_6$		2		[1]	68.5	4.35, 4.44	4.15	168—170	9.49, 9.46	9.48	174—176	26.57, 26.35	26.46
—$(CH_2)_2O(CH_2)_2$—		2	71—73	[1]	71.7	4.28, 4.13	4.30	199—200.5	9.79, 9.69	9.80	155—156	26.89, 26.78	27.15
CH_3	CH_3	3		185(3)	75	4.43 [2]	4.71	142	10.57, 10.56	10.62	185	29.02	28.49
C_2H_5	C_2H_5	3		185—190(4)	61	4.64 [3]	4.32	168	9.69, 9.57	9.80	163	27.43	27.16
C_2H_5	C_2H_5	4		[1]	72	[4]		134.5—136.5	9.33, 9.28	9.43	136.5—138	26.51, 26.53	26.36
—$(CH_2)_5$—		4		[1]	68	4.06, 4.20 [5]	3.99	152.5—154.0	9.07, 8.89	9.14	169—170.5	26.08, 26.12	25.71
—$(CH_2)_6$		4		[1]	76.5	[6]		132—133.5	9.01, 9.12	8.82	169.5—171	24.83, 24.70	25.01
—$(CH_2)_2O(CH_2)_2$—		4		[1]	65.1			146—148	8.94, 8.93	9.09	164—166	25.87, 25.91	25.61

1 Substance not fractionated.

2 Found %: C 60.60; H 7.93; $C_{15}H_{23}O_5N$. Calculated %: C 60.58; H 7.79.

3 Found %: C 63.21; H 8.78. $C_{17}H_{27}O_5N$. Calculated %: C 62.96; H 8.36.

4 Found %: C 63.95, 64.06; H 8.70, 8.46. $C_{18}H_{29}O_5N$. Calculated %: C 63.71; H 8.61.

5 Found %: C 65.85, 65.95; H 8.70, 8.85. $C_{20}H_{31}O_5N$. Calculated %: C 65.72; H 8.55.

6 Found %: C 61.19, 61.28; H 7.72, 7.75. $C_{18}H_{27}O_6N$. Calculated %: C 61.17; H 7.70.

7 Literature data [8]: m. p. 159°.

Pharmacological tests on the prepared compounds, carried out by N. V. Kaverina and I. N. Pidevich in the laboratory of special pharmacology of the institute, showed that a hypotensive effect is not manifested and that only a portion   of the compounds possess a moderate sedative action. No relation was found between the degree of similarity of the structure of the preparations to the structure of reserpine and their sedative activity; for example, compound (II) (n = 4, R' = R'' = C_2H_5), which is completely represented in the structure of reserpine, was found to be considerably less active than (II) (n = 3, R' = R'' = C_2H_5), possessing 1/4 of the activity of reserpine (see [1]). Some of the investigated compounds, for example, the methiodide of (II) (n = 4, R' = R'' = C_2H_5) were capable of preventing the development of experimental disturbances of the cardiac rhythm. The results of the pharmacological tests will be presented in more detail elsewhere.

EXPERIMENTAL

β-(N-Methylpiperidyl)-carbinyl ester of 3,4,5-trimethoxybenzoic acid. A solution of 3.9 g β-(N-methyl-piperidyl)-carbinol [9] in 20 ml benzene was stirred dropwise into a boiling solution of 6.9 g 3,4,5-trimethoxybenzoyl chloride [2] in 40 ml benzene. The heated reaction mass was stirred 6 hr, after which it was cooled and left for 12 hr. The resulting crystals of hydrochloride were filtered off and washed with benzene. There was obtained 8 g of compound with m.p. 139-140°.

4 g hydrochloride was dissolved in 20 ml water, the solution was acidified with hydrochloric acid and extracted with ether. The ethereal extracts were rejected. The solution was boiled 3 min with active carbon and filtered. Aqueous ammonia was added until the liquid was alkaline to phenolphthalein. The resulting oil was extracted with ether, the ethereal extract was dried with magnesium sulfate, the ether was driven off and the residue was distilled in vacuo. B. p. 186° (2 mm). Yield 1.8 g.

Found %: C 62.73; H 7.87; N 4.39. $C_{17}H_{25}O_5N$. Calculated %: C 63.06; H 7.79; N 4.33.

Hydrochloride. To 0.5 g base was added 10 ml water and 0.1 N hydrochloric acid until liquid was weakly acid to Congo. The solution was filtered and evaporated in vacuo; the solid residue was recrystallized from acetone. M. p. 146°. Easily soluble in water and alcohol, sparingly soluble in acetone and ether.

Found %: Cl 9.82, 9.95. $C_{17}H_{25}O_5N \cdot HCl$. Calculated %: Cl 9.86.

Methiodide. To a solution of 3 g of the base in 30 ml methanol was added 3 g methyl chloride. The mixture was heated 3 hr on a water bath, after which the methanol was driven off. The residue was mixed with 25 ml acetone, filtered, washed with acetone, and recrystallized from methanol to give 3 g methiodide with m.p. 195°.

Found %: I 27.30, 27.31. $C_{17}H_{25}O_5N \cdot CH_3I$. Calculated %: I 27.31.

γ-Diethylaminopropyl ester of 3,4,5,-trimethoxybenzoic acid. A mixture of 2.34 g dried sodium salt of 3,4,5-trimethoxybenzoic acid, 1.5 g γ-diethylaminopropyl chloride and 50 ml toluene was refluxed 8 hr. The sodium chloride was then filtered off and washed with toluene. The toluene solutions were twice extracted with 1 N hydrochloric acid (in 10 ml portions). The aqueous extract was made alkaline with ammonia solution and extracted with ether. The residue after removal of the ether was fractionated in vacuo to give 2 g of substance with b. p. 185-190° at 4 mm (see table).

2-(N-Hexamethyleneimino)-1-ethanol. A solution of 39.7 g hexamethyleneimine in 50 ml benzene was added dropwise in the course of half an hour to a boiling solution of 21.8 g ethylenebromohydrin in 50 ml benzene. The reaction mixture was stirred 8 hr on a boiling water bath. The next day the precipitate of hexamethyleneimine hydrobromide was filtered off, the benzene was distilled off, and the residue was distilled in vacuo in a nitrogen stream to give 19.1 g (67%) 2-(N-hexamethyleneimino)-1-ethanol.

B.p. 87° at 7 mm, n_D^{20} 1.4828, d_4^{20} 0.9692, MR_D 42.20; calc. 42.41.
Found %: C 67.17, 67.06; H 11.95, 12.07; N 10.00, 10.01. $C_8H_{17}ON$. Calculated %: C 67.11; H 11.96; N 9.78.

4-(N-Hexamethyleneimino)-1-butanol. In the course of 30 min a solution of 29.8 g hexamethyleneimine in 30 ml benzene was added dropwise to a boiling solution of 27.5 g 4-bromo-1-butyl acetate [3] in 30 ml benzene. After addition had been completed, the boiling mixture was stirred 8 hr and then cooled. The precipitate of hexamethyleneimine hydrobromide was filtered off and the benzene was taken off in a nitrogen streatm. To

the residual oily liquid was added 100 ml water and hydrobromic acid until a weakly acid reaction to Congo was obtained. The solution was boiled 30 min with addition of active carbon and then filtered hot. After cooling, it was made alkaline with concentrated ammonia solution and extracted with ether. The extract was dried with magnesium sulfate. The oil remaining after the ether had been driven off was fractionated in vacuo to give 17.7 g (69.2%) 4-(N-hexamethyleneimino)-1-butanol with b. p. 110-112° at 4 mm.

$n^{20}D$ 1.4813, d^{20}_4 0.9566, MRD 50.93; calc. 51.64.

Found %: C 69.85, 69.70; H 12.53, 12.56; N 7.92, 7.97. $C_{10}H_{21}ON$. Calculated %: C 70.09; H 12.36; N 8.18.

The following compounds were prepared in similar fashion:

4-(N-Morpholino)-1-butanol (yield 85%):

B. p. 114-116° at 4 mm, $n^{20}D$ 1.4716, d^{20}_4 0.9971. Literature data [4]: b. p. 116.5-117.5° at 5 mm, $n^{14}D$ 1.4745, d^{25}_4 1.018.

4-(N-Piperidyl)-1-butanol (yield 78%):

B. p. 127-129° at 18 mm, $n^{20}D$ 1.4740, d^{20}_4 0.9450. Literature data [5]: b. p. 133-134° at 20 mm.

4-Diethylamino-1-butanol (yield 57.5%):

B. p. 133-134° at 21 mm, $n^{20}D$ 1.4481, d^{20}_4 0.871. Literature data [6]: b. p. 90-92° at 7-9 mm, $n^{20}D$ 1.4474, d^{20}_4 0.876.

SUMMARY

12 dialkylaminoalkyl esters of 3,4,5-trimethoxybenzoic acid were prepared for comparative pharmacological investigations and were characterized.

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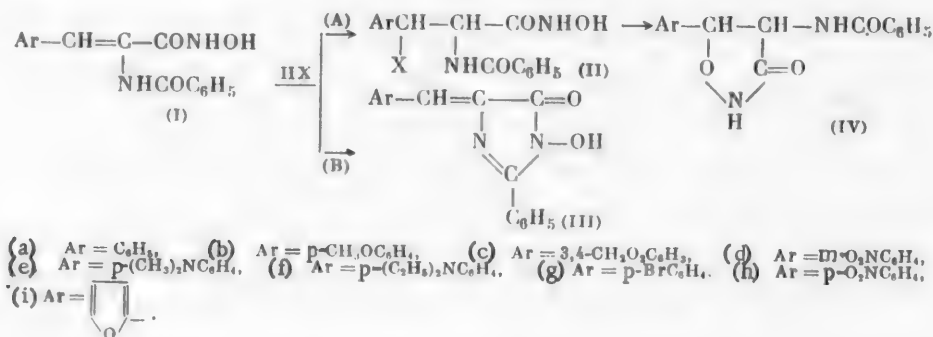
CYCLOSERINE AND RELATED COMPOUNDS

V. CYCLIZATION OF α-BENZOYLAMINO-β-ARYLACRYLOHYDROXAMIC ACIDS

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In the preceding paper [1], we described a general method of synthesis of α-benzoylamino-β-arylacrylo-hydroxamic acids. Cyclization of these compounds could open out a route to the synthesis of 5-substituted 4-amino-3-isoxazolidones, i.e., analogs of the antibiotic cycloserine.

Reaction of α-benzoylamino-β-arylacrylohydroxamic acids (I) with hydrogen halides (HCl, HBr) would be expected to lead to the corresponding α-benzoylamino-β-aryl-β-halopropionohydroxamic acids (II), which by treatment with alkalies should be converted to 5-aryl-4-benzoylamino-3-isoxazolidones (III). It is also known, however, that compounds (I) can cyclize by another route when treated with hydrochloric acid, namely with formation of 2-phenyl-5-arylidene-3-ol-4-ones (IV).


(a) Ar = C₆H₄, (b) Ar = p-CH₃OC₆H₄, (c) Ar = 3,4-CH₃O₂C₆H₃, (d) Ar = m-O₂NC₆H₄, (e) Ar = p-(CH₃)₂NC₆H₄, (f) Ar = p-(C₂H₅)₂NC₆H₄, (g) Ar = p-BrC₆H₄, (h) Ar = p-O₂NC₆H₄, (i) Ar =

The second possibility (route B) was demonstrated by Shaw and McDowell [2] in the case of cyclization of α-benzoylamino-β-phenyl- and α-benzoylamino-β-p-methoxyphenylacrylohydroxamic acids to the corresponding imidazolinolones (IV) in yields of 50 and 16% respectively by boiling with aqueous hydrochloric acid.

Reasoning that the character of the substituent in the aromatic nucleus could influence the direction of the reaction (A or B), we closely investigated the cyclization of α-benzoylamino-β-arylacrylohydroxamic acids. Treatment of the latter with hydrogen chloride or bromide in various solvents (methanol, dioxane, acetic acid) over a wide temperature range (–50 to + 100°) led to facile cyclization with formation of imidazolinolones in nearly quantitative yield. In no case did we observe the formation of products of addition of hydrogen halides of the type of (II). It would, therefore, appear that route B is followed during formation of (I) regardless of the nature of the substituent at the nucleus. It was also found that cyclization of (I) to (IV) goes so easily that a mineral acid does not even need to be present in some cases; it suffices to have catalytic quantities of acetic

acid; sometimes, indeed, the reaction goes under the influence of the hydroxamic acid itself (autocatalysis).

The mechanism of this reaction is probably similar to that of azlactonization of α-actylaminoacids. Cyclization to the imidazolinolone derivative (IV) goes with sufficient facility only in the case of unsaturated acylaminohydroxamic acids of the type of (I); attempts to perform this reaction with saturated analogs, α-benzoyl-β-arylalaninohydroxamic acids whose preparation was described in the preceding communication [1], gave negative results. Instead of cyclization, we observed only hydrolysis of the hydroxamic grouping. As is well known [3, 4], azlactonization ges with especial facility in the case of unsaturated acylaminoacids. This is presumably because the double bond facilitates the action of the electrophilic aromatic ring on the nucleophilic acylamino group which probably enters into reaction in the enolimido form (cf. [5]). In that event we could represent the cyclization in presence of acid by the mechanism:
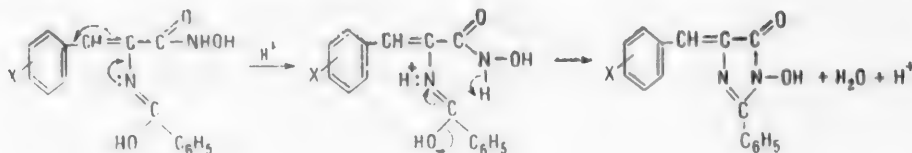

The nature of the substituent does not influence the over-all reaction course, but probably influences the first step — protonization of the imido nitrogen; thus the introduction of a nucleophilic substituent facilitates cyclization, while an electrophilic substituent in the para-position hinders the reaction. In the second step (ring closure) the nature of the substituent is evidently not an important factor since the influence of the positive charge brought in by the proton is very much stronger than that of a charge transmitted by a substituent in a conjugated chain.

The 2-phenyl-5-arylideneimidazoline-$\Delta^{1,2}$-ol-3-ones-4 (IV) that we prepared are yellow or orange, crystalline substances, easily soluble in organic solvents and poorly soluble in water. In aqueous solutions of caustic alkalies they form poorly soluble, colored potassium and sodium salts. Compound (IV) is characterized by high stability, remaining unchanged when boiled with hydrochloric acid and developing an odor of benzaldehyde only when boiled with caustic alkali solutions (Fig. 1 and 2).
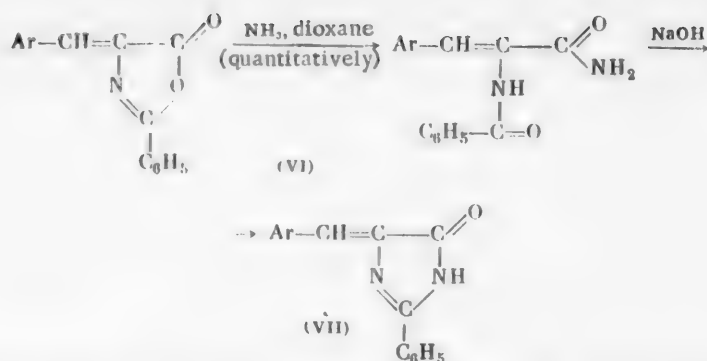
The study of the antibacterial activity of imidazolinolones is of considerable interest since, as cyclic hydroxamic acids, they are analogs of the antibiotics aspergillic acid [6] and nocardamine [7], which are very active but fail to find practical application due to their high toxicity. It was found that our compounds of the type of (IV) possess high bacteriostatic action in vitro (in concentrations of 10-50 γ/ml) both against gram-positive and gram-negative bacteria, including intestinal bacteria and (in some cases) Microbacterium tuberculosis. Compounds (IVa), (IVc) and (IVf) merit special attention.

The activity of this entirely new group of antimicrobial agents is evidently associated with the presence of the —CON—R grouping (present also in aspergillic acid and nocardamine), since a change in this part of
      |
     OH
the molecule leads to complete loss of activity. Thus, methylation of the hydroxyl group in (IVa) and (IVb) by methyl iodide in methanol gave 2-phenyl-5-benzylidene- and 2-phenyl-5-(p-methoxybenzylidene)-3-methoxyimidazolin-$\Delta^{1,2}$-ones-4 (V) which are completely devoid of activity.
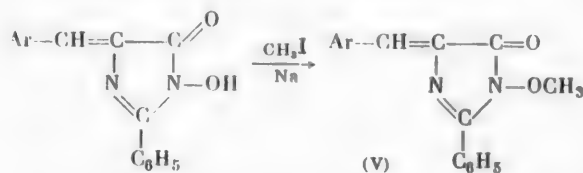
Absence of activity also distinguishes the 2-phenyl-5-benzylidene- and 2-phenyl-5-(p-methoxybenzylidene)-imidazolin-$\Delta^{1,2}$-ones-4 (VII) obtained by cyclization with aqueous caustic alkali of the amides of the corresponding α-benzoylaminocinnamic acid [8, 9].

$$Ar-CH=C-C\overset{\displaystyle O}{\underset{\displaystyle }{\diagup}} \xrightarrow[\text{(quantitatively)}]{NH_3,\ dioxane} Ar-CH=C-C\overset{\displaystyle O}{\underset{\displaystyle NH_2}{\diagup}} \xrightarrow{NaOH}$$

(VI)

$$\rightarrow Ar-CH=C-C\overset{\displaystyle O}{\underset{\displaystyle }{\diagup}}$$

(VII)

In our discussion of the reaction mechanism, we suggested that the aromatic ring decisively governs the direction of the reaction. With the objective of confirming this hypothesis and of establishing the possibility of utilization of β-substituted α-acylaminoacrylohydroxamic acids for the synthesis of analogs of cycloserine, we studied (in one case only) the reaction of α-benzoylaminoacrylohydroxamic acids, containing an aliphatic
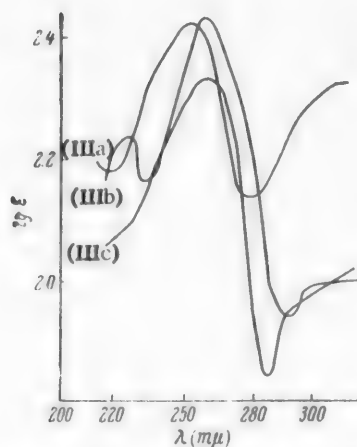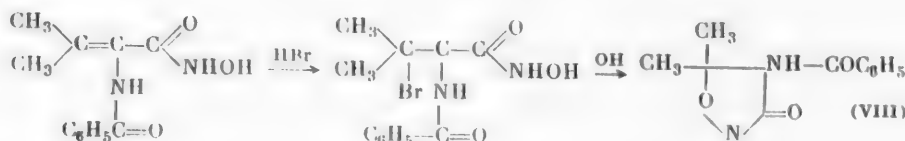

Fig. 1. Ultraviolet absorption spectrum of 2-phenyl-5-arylideneimidazoline-$\Delta^{1,2}$-ol-3-ones-4. Explanation in text.

radical in the β-position, with hydrogen halides. It was found that an entirely different reaction course is followed, namely route (A). Treatment of α-benzoylamino-β,β-dimethylacrylohydroxamic acid with hydrobromic acid in acetic acid gave α-benzoylamino-β-bromo-β,β-dimethylpropionohydroxamic acid, which under the action of potassium hydroxide, sodium hydroxide or sodium carbonate gives 5,5-dimethyl-4-benzoylaminoisoxazolidone-3 (VIII).

The structure of (VII) is confirmed by its insolubility in acids and its solubility in caustic alkalies, as well as by the coloration with sodium nitroprusside which is characteristic of compounds of the 4-amino-3-isoxazolidone series [10]. Further confirmation of the structure was obtained with the help of the ultraviolet absorption spectrum which is similar to that of its closest analog — 4-benzoylamino-3-isoxazolidone (benzoylcycloserine) (IX) (see Fig. 3).

The course of the reaction of β-substituted α-acylaminoacrylohydroxamic acid with hydrogen halides consequently varies with the nature of the substituent in the β-position. We are now engaged in a closer investigation of this field.

$$\underset{CH_3}{\overset{CH_3}{\diagdown}}C=C-C\overset{\displaystyle O}{\underset{\displaystyle NHOH}{\diagup}} \xrightarrow{HBr} \underset{CH_3}{\overset{CH_3}{\diagdown}}C-C-C\overset{\displaystyle O}{\underset{\displaystyle NHOH}{\diagup}} \xrightarrow{OH} CH_3\overset{\displaystyle CH_3}{\underset{\displaystyle }{|}}NH-COC_6H_5$$

(VIII)

EXPERIMENTAL

2-Phenyl-5-arylideneimidazolin-$\Delta^{1,2}$-ol-3-ones-4 (III). 0.01 mole α-benzoylamino-β-arylacrylohydroxamic acid was dissolved in 30-50 ml of a suitable solvent, and 0.005-0.01 mole hydrogen halide (or acetic acid) was added. In case of α-benzoylamino-β-(p-dimethylaminopiperidyl)- and -(p-diethylamino-piperidyl)-acrylohydroxamic acids (Ie and If) the quantity of hydrogen halide taken was 0.015-0.02 mole. The mixture was stood at room temperature or heated for a short time. The resulting precipitate was filtered, washed, and dried in the air. The filtrate was diluted with water which brought down a supplementary quantity of

imidazolinolone. Details of reaction conditions, yields and constants of the products obtained by this method are given in the table.

2-Phenyl-5-benzylidene-3-methoxyimidazoline-$\Delta^{1,2}$-one-4 (Va). 2.64 g 2-phenyl-5-benzylideneimidazoline-$\Delta^{1,2}$-ol-3-one-4 was dissolved in 50 ml methanol containing 0.01 mole sodium methoxide; 1.5 ml methyl iodide was added and the mixture was boiled 2 hr. The solution was cooled and diluted with 1 N alkali. The yellow precipitate was filtered and washed with 1N alkali (for removal of starting substance) and with water. Yield 1.8 g (65%); m. p. 115-116° (from alcohol).

Found %: C 73.35; H 5.12; N 10.22. $C_{17}H_{14}O_2N_2$. Calculated %: C 73.37; H 5.06; N 10.06.

The same procedure was used for preparation of 2-phenyl-5-(p-methoxybenzylidene)-3-methoxyimidazoline-$\Delta^{1,2}$-one 4 (Vc); yield 73%; m. p. 122-124° (from alcohol).

Found %: C 70.20; H 5.08; N 8.74. $C_{18}H_{16}O_3N_2$. Calculated %: C 70.19; H 5.22; N 9.08.

Amides of α-benzoylaminocinnamic acids. 10 g 2-phenyl-5-benzylideneoxazolone was dissolved by stirring in 150 ml dry dioxane containing 3 g ammonia. After an hour the whole of the substance had gone into solution. The reaction mixture was diluted with 400 ml water and the snow white precipitate was filtered and
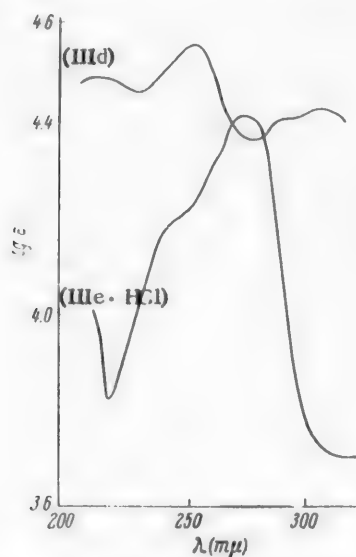

Fig. 2. Ultraviolet absorption spectrum of 2-phenyl-5-(m-nitrobenzylidene)-imidazolin-$\Delta^{1,2}$-ol-3-4-one (IIId) and of the hydrochloride of 2-phenyl-5-(p-dimethylaminobenzylidene)-imidazolin-$\Delta^{1,2}$-ol-3-one-4 (hydrochloride of IIIe).
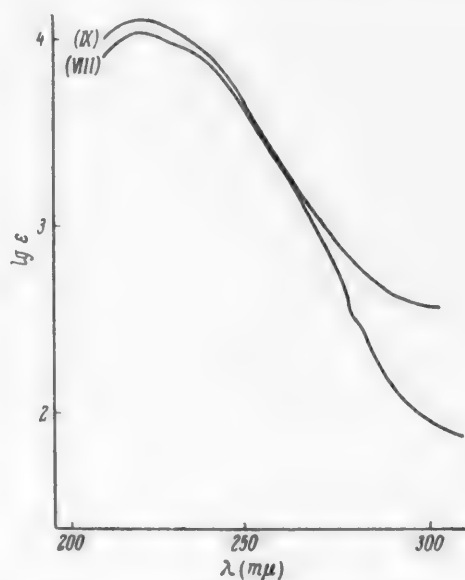

Fig. 3. Ultraviolet absorption spectrum of benzoylcycloserine (IX) and of 5,5-dimethylbenzoylcycloserine (VIII).

washed with water. The yield of α-benzoylcinnamamide (VIa) was 10 g (94%); m. p. 168-169° (from dioxane). Literature data [8]; m. p. 168°.

α-Benzoylamino-p-methoxycinnamamide (VIb) was similarly prepared in quantitative yield; m. p. 190-192°; solidifies as yellow needles at 215° and again melts at 265°.

2-Phenyl-5-benzylideneimidazoline-$\Delta^{1,2}$-one-4. 2 g α-benzoylaminocinnamamide was heated on a water bath with 30 ml 5% sodium hydroxide solution. After 45 min the yellow precipitate was cooled, filtered, and recrystallized from alcohol. Yield of 2-phenyl-5-benzylideneimidazoline-$\Delta^{1,2}$-one-4 was 96%. M.p. 270° (same as reported in the literature [8]).

2-Phenyl-5-p-methoxybenzylideneimidazoline-$\Delta^{1,2}$-one-4 was similarly prepared. Yield 84%; m. p. 277-279°.

2-Phenyl-5-arylidenimidazolin-$\Delta^{1,2}$-ol-3-ones-4

$$Ar-CH=C-\!\!\!\!\underset{\underset{\overset{|}{C_6H_5}}{N}}{\overset{|}{\underset{\diagdown}{}}}\!\!\!C=O$$

$$\diagdown_{C-N-OH}$$
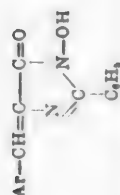
Ar	Solvent	Catalyst	Reaction temperature	Duration of reaction (hours)	Yield (%)	M.p. (solvent from which recrystallized)	Content (%)								Remarks
							C found	C calc.	H found	H calc.	N found	N calc.	haloid found	haloid calc.	
C_6H_5	CH_3OH	HBr	20°	3	91										
C_6H_5	CH_3COOH	HBr	20	3	90										
C_6H_5	CH_3COOH	HCl	20	4	96										
C_6H_5	CH_3OH	HCl	20	12	98	202—204° (w.decomp., alcohol)	72.96	72.72	4.75	4.55	10.78	10.61	—	—	
C_6H_5	Dioxane	HCl	50—60	5 minutes	76										
C_6H_5	CH_3OH	HCl	50—70	2 minutes	87										
$p\text{-}CH_3OC_6H_4$	CH_3OH	HCl	50—60	2 minutes	100	225—227 (alcohol)	69.38	69.67	5.01	4.81	9.58	9.52	—	—	
$3,4\text{-}CH_2O_2C_6H_3$	CH_3OH	—	20	0.5	97	220—222 (спирт)	66.22	66.49	4.04	3.89	8.92	9.08	—	—	
$6.4\text{-}CH_2O_2C_6H_3$	CH_3OH	HCl	60	0.5	80	197—198 (alcohol)							—	—	
$m\text{-}NO_2C_6H_4$	CH_3OH	HCl	20	0.5	73	218—220 (alcohol + chloroform)	62.72	62.46	3.61	3.44	13.48	13.46	—	—	
$p\text{-}(CH_3)_2NC_6H_4$ *	CH_3OH	HCl	60	0.75	84	215—216 (alcohol)	70.89	70.35	5.76	5.56	13.62	13.66	Cl 10.32	Cl 10.41	Hydro-chloride
$p\text{-}(C_2H_5)_2NC_6H_4$ *	CH_3OH	HCl	60	0.75	85	175—178	71.90	71.66	6.41	6.27	—	—	—	—	Base
$p\text{-}BrC_6H_4$	CH_3OH	HCl	60	3.5	77	256—257	56.42	56.00	3.38	3.23	11.00	11.02	23.32**	23.37	Base
$\alpha\text{-}Furyl$	C_2H_5OH	—	80	6	12)	225—227 (alcohol + acetone)	66.53	66.13	4.26	3.93	—	—	—	—	
$\alpha\text{-}Furyl$	C_2H_5OH	CH_3COOH	80	6	82)										

* The hydrochloride prepared by this reaction was dissolved in 50% methanol and made alkaline until a test of the extract was negative. The base was then filtered, washed with water and dried.

** Analysis for bromine.

5,5-Dimethyl-4-benzoylamino-3-oxazolidone (VII). 4.7 g α-benzoylamino-β,β-dimethylacrylohydrox-amic acid was dissolved in 100 ml methanol, and 5 ml of 40% solution of hydrobromic acid in glacial acetic acid was added. The mixture was stood 2 hours at room temperature. 25 ml of 40% sodium hydroxide solution was then stirred in quickly. The mass was boiled 5-10 min and cooled. Water was added to dissolve com-pletely the sodium bromide, and the liquid was acidified to pH 5. After a few minutes a voluminous precipi-tate of 5,5-dimethyl-4-benzoylamino-3-isoxazolidone came down. It was filtered and washed with water, meth-anol and ether. Yield 4.2 g (89%); m. p. 170-172°.

Found %: N 11.63. $C_{12}H_{14}O_3N_2$. Calculated %: N 11.91.

Compound (VII) can be prepared without intermediate isolation of α-benzoylamino-β,β-dimethylacrylo-hydroxamic acid from 2-phenyl-5-isopropylideneoxazolone in 80% yield.

The compound forms colorless plates; it does not give a coloration with salts of trivalent iron and gives a characteristic blue color with nitroprusside. The ultraviolet absorption spectrum is identical with the spectrum of N-benzoyl-cycloserine synthesized by the known method (see Fig. 3).

Cyclization with sodium hydroxide in the cold is completed in 1-1.5 hour, and with potassium hydroxide and sodium carbonate at the boil in 3-5 min. Yield of 5,5-dimethyl-4-benzoylamino-3-isoxazolidone 80%.

SUMMARY

1. A method was developed for the synthesis of 2-phenyl-5-arylideneimidazoline-$\Delta^{1,2}$-ol-3-ones-4 by cyclization of β-aryl- α-benzoylaminoacrylohydroxamic acids with hydrogen halide in alcoholic or acetic acid solution (yields from 73% to quantitative). It was shown that the prepared compounds possess high bacterio-static activity.

2. It was shown that the bacteriostatic activity disappears when the N-hydroxyl group in 2-phenyl-5-arylideneimidazoline- $\Delta^{1,2}$-ol-3-ones-4 is replaced by the methoxy group or a hydrogen atom.

3. It was shown that treatment of β,β-dimethyl-α-benzoylaminoacrylohydroxamic acid with hydrogen bromide in acetic acid causes the reaction to go in a different direction, and treatment of the reaction product with caustic alkali gives 5,5-dimethyl-4-benzoylamino-3-isoxazolidone.

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•See C.B. Translation.

••Original Russian pagination. See C.B. Translation.

CYCLOSERINE AND RELATED COMPOUNDS

## VI. SYNTHESIS OF ANALOGS OF CYCLOSERINE WITH A SUBSTITUTED AMINO GROUP

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In connection with a study of the relation between chemotherapeutic activity and structure in a new class of compounds — derivatives of 4-amino-3-isoxazolidone — it was of interest to make use of our method [1, 2] of synthesis of analogs of cycloserine containing a substituted amino group. Before this investigation had been completed, F. Sorm and co-workers [3] published a paper on the synthesis of two representatives of this series (N-benzylcycloserine and N-benzhydrylcycloserine) prepared by another route.

For the synthesis of cycloserine analogs, we used the scheme that we previously used for the synthesis of the natural antibiotic itself.
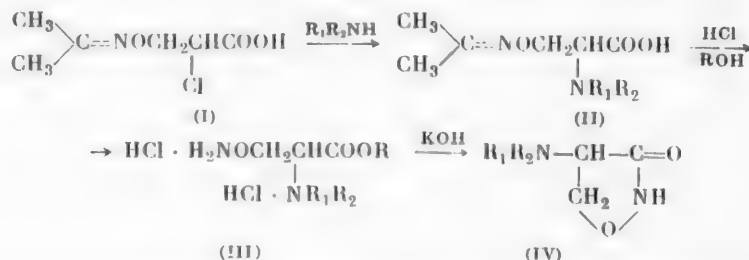
It should be noted that difficulties arise when the preparation of N-substituted derivatives of β-isopropyl-idene-aminohydroxyalanines (II) is attempted by another route. For example, direct alkylation of β-isopropyl-idene-aminohydroxyalanine gives a difficulty resolvable mixture of products of all stages of alkylation.

As the starting substance for synthesis of N-substituted analogs of cycloserine, we took α-chloro-β-isopropylidene-aminohydroxypropionic acid (I), one of the intermediates in the synthesis of cycloserine [2]. Reaction of acid (I) with various amines in aqueous and alcoholic media failed to give detectable quantities of derivatives of alanine (II). β-Isopropylidene-aminohydroxyalanine itself could not be obtained by amination of the chloroacid (I) in an aqueous or alcoholic medium [1, 2].

Amination of the chloroacid (I) was studied in inert solvents as well as with heating with excess of the amine in the absence of solvent. The latter variant gave the most satisfactory result.

Chloroacid (I) was aminated with methylamine, β-phenylethylamine, benzylamine, piperidine and morpholine, all taken in excess in relation to the chloroacid. The reaction was found to be a general one, but special conditions had to be employed for separation of each compound.

Methylamine, benzylamine, phenylethylamine and piperidine gave crystalline α-methylamino-, α-ben-zylamino-, α-phenylethylamino- and α-piperidyl-β-isopropylideneaminohydroxypropionic acids [(II), R$_1$= H,

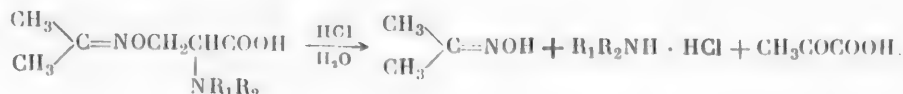$R_2 = CH_3$; $R_1 = H$, $R_2 = C_6H_5CH_2$; $R_1 = H$, $R_2 = C_6H_5CH_2CH_2$; $R_1, R_2 = -(CH_2)_5$] in yields of 25 to 70%. Reaction of chloroacid (I) with morpholine gave an oily α-aminoacid which could not be purified and crystallized in spite of repeated attempts.

The next step in the synthesis of analogs of cycloserine was transition from aminoacids (II) to the dihydrochlorides of esters of N-substituted α-amino-β-aminohydroxypropionic acids (III). As had been shown earlier [2], optimum conditions for preparation of the dihydrochloride of a β-aminohydroxyalanine are established during hydrolysis of the aminoacid with a mixture of hydrochloric acid and alcohol prior to esterification. Hydrolysis of α-methylamino-β-isopropylidene-aminohydroxypropionic acid (II, $R_2 = CH_3$, $R_1 = H$) gave us a 54% yield of the dihydrochloride (III; $R_2 = CH_3$, $R_1 = H$) in the crystalline form. Cyclization of the dihydrochloride under our previous conditions of synthesis of cycloserine [2], i.e., treatment with methanolic solution of potassium hydroxide prior to acidification with acetic acid, gave 4-methylamino-3-isoxazolidone (IV; $R_2 = CH_3$, $R_1 = H$) in a yield of up to 60%.

Hydrolysis of the other aminoacids (II) under similar conditions with a mixture of concentrated hydrochloric acid and alcohol followed by esterification gave the corresponding dihydrochlorides in the form of uncrystallizable oils which could not be obtained in the analytically pure state. More drastic treatment of the dihydrochlorides (III) led to partial breakdown of the compounds. This behavior demonstrated the relative instability of these compounds and indicated a characteristic influence of the labile β-aminohydroxy group in the molecule of the α-aminoacid. For preparation of other analogs of cycloserine (IV), we made use of the oily dihydrochlorides without bringing them to the analytically pure state. After treatment of the latter with alcoholic potassium hydroxide under the usual conditions, paper chromatography [mobile phase: tert-butanol n-butanol, 1 N NH_4OH (1:1:5)] revealed the presence of products of cyclization for all of the three dihydrochlorides (containing the benzyl, phenethyl and piperidino radicals). Development with sodium nitroprusside gave three characteristic blue traces; the values of R_f were in the same region (from 0.28 to 0.57) and corresponded to the R_f of cycloserine (0.12) which is more hydrophilic. After a number of difficulties had been overcome, we succeeded in isolating crystalline 4-benzylamino-3-isoxazolidone (IV; $R_2 = C_6H_5CH_2$, $R_1 = H$) and 4-phenylethyl-3-isoxazolidone (IV; $R_2 = C_6H_5CH_2CH_2$, $R_1 = H$) in yields of 10-12% calculated on the original aminoacid (II).

All attempts to isolate a crystalline substance after cyclization of the dihydrochloride containing a piperidine radical [III; $R_1R_2 = -(CH_2)_5$] were unsuccessful. Examination by paper chromatography (see above) nevertheless demonstrated the formation under these conditions of an analog of cycloserine containing the piperidine ring [IV; $R_1R_2 = -(CH_2)_5$].

Investigation of the products of hydrolysis of α-piperidyl-β-isopropylideneaminohydroxypropionic acid [II; $R_1R_2 = -(CH_2)_5$] revealed that one of the products of this hydrolysis was piperidine hydrochloride which we isolated in crystalline form in a yield of about 40%. It was identified by a mixed melting point test. Examination of the products of hydrolysis of aminoacids (II) containing the benzyl and phenethyl radicals showed that the dihydrochlorides (III) were accompanied by the hydrochlorides of benzylamine and phenylethylamine in yields of 7 to 10%. Hydrolysis of (II) goes in more than one direction and is complicated by a secondary reaction which predominates in the case of the piperidine derivative [II; $R_1R_2 = -(CH_2)_5$]. Formation of the hydrochloride of the amine during acid hydrolysis of N-substituted β-isopropylidene-aminohydroxy-α-aminopropionic acid indicates that this secondary reaction is an acid deamination evidently proceeding according to the equation

$$\begin{array}{c} CH_3 \\ CH_3 \end{array}\!\!\!\!>\!C\!=\!NOCH_2CHCOOH \xrightarrow[H_2O]{HCl} \begin{array}{c} CH_3 \\ CH_3 \end{array}\!\!\!\!>\!C\!=\!NOH + R_1R_2NH \cdot HCl + CH_3COCOOH.$$
$$\underset{NR_1R_2}{|}$$

This secondary process is especially conspicuous in the case of an N,N-disubstituted α-aminoacid containing the aminohydroxy group in the β-position. It goes to a lesser degree when the amino group contains only one radical (this is evident from a comparison of the yields of piperidine hydrochloride and benzylamine hydrochloride; see above). It may even take place with β-isopropylidene-aminohydroxyalanine itself, since in hydrolysis of this compound with a mixture of hydrochloric acid and alcohol [2], we likewise observed the formation of some ammonium chloride.

It may be thought that the first step in an acid medium is formation of the hydrochloride of the amino-acid due to protonization of the α-amino nitrogen, and that attack of the proton, directed most probably at the oxygen of the oxime group, leads to a normal β-elimination of the oxime. This process would lead to a derivative of α-aminoacrylic acid, which undergoes hydrolysis in the acid medium.

In fact, heating of the hydrochloride of α-piperidyl-β-isopropylideneaminohydroxypropionic acid in butyl alcohol in presence of catalytic quantities of hydrogen ion gave a 40% yield of piperidine hydrochloride, while a qualitative test with sodium nitroprusside demonstrated the presence of pyruvic acid.

This experiment qualitatively confirms the facile deamination of α-amino-substituted β-isopropylidene-aminohydroxypropionic acids. A decomposition of this type may have a wider significance for α-amino-acids with an oxygen-containing group in the β-position (serine, threonine), and this aspect undoubtedly merits close consideration.

For the purpose of comparison of the cycloserine analogs that we prepared, we repeated the synthesis of N-benzylcycloserine by the method of Sorm and co-workers [3], but with different conditions of cyclization of α-benzylamino-β-chloropropionohydroxamic acid to 4-benzylamino-3-isoxazolidone.
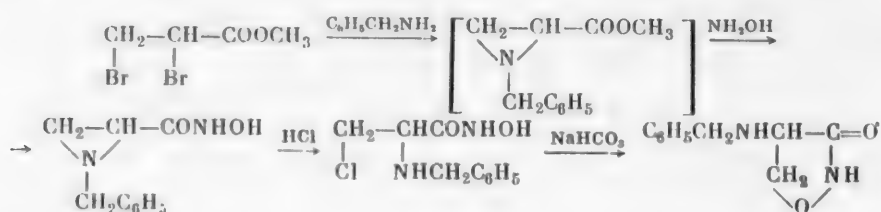
By carrying out the cyclization with concentrated aqueous sodium bicarbonate solution, we succeeded in raising the yield of 4-benzylamino-3-isoxazolidone from 28 to 50%. We used this reaction procedure for synthesis of the previously unknown 4-phenylethylamino-3-isoxazolidone, applying our modified cyclization conditions. The so-prepared 4-benzyl- and 4-phenylethylamino-3-isoxazolidones were fully identical with specimens obtained by our earlier method (see above) when tested by mixed melting points and paper chromatography.

4-Methyl-, 4-benzyl- and 4-phenylethylamino-3-isoxazolidones are colorless, crystalline, stable substances. Their chemical behavior is the same as that of cycloserine itself.

We have also discovered a new method of synthesis of 4-N-substituted homologs of 3-isoxazolidone, based on formation of Schiff bases of cycloserine followed by their hydrogenation (see next paper in this series).

EXPERIMENTAL

Preparation of α-Amino-substituted β-Isopropylidene-aminohydroxypropionic Acids (II)

α-Methylamino-β-isopropylidene-aminohydroxypropionic acid. 45 g α-chloro-β-isopropylidene-amino-hydroxypropionic acid was dissolved in 150 ml liquid methylamine. 1 g ammonium nitrate was added and the mixture heated in an autoclave for 20 hr at 50-60°, after which it was evaporated to dryness in vacuo. The colorless, crystalline product was a mixture of N-methyl-β-isopropylidene-aminohydroxyalanine and methyl amine hydrochloride. It was dried in a vacuum-desiccator over phosphorus pentoxide. Three recrystallizations from isopropyl alcohol with addition of water until the substance dissolved completely gave 20 g (40%) α-methylamino-β-isopropylidene-aminohydroxypropionic acid with m.p. 192-193° (decomp.), free of chlorine ion. R_f 0.74 (descending chromatogram; Whatman no. 1; 48 hr, mobile phase: butanol-acetic acid-water 4:3:3; development with ninhydrin at 100°).

Found %: N 16.10. $C_7H_{14}O_3N_2$. Calculated %: N 16.08.

α-Phenylethylamino-β-isopropylidene-aminohydroxypropionic acid. A mixture of 23.4 g α-chloro-β-isopropylidene-aminohydroxypropionic acid and 78 g freshly distilled phenylethylamine was stirred on a boiling water bath for 6.5 hr. The mass was then cooled, 100 ml ether was added, and the precipitate was filtered,

washed with ether, dissolved in the minimum quantity of boiling 50% aqueous alcohol and again filtered. The aqueous alcoholic filtrate was stood at 5-10°. Crystals came down after 48 hour and were filtered, washed with cold alcohol and with ether. Yield 20-22 g N-phenylethyl-β-isopropylidene-aminohydroxypropionic acid with m.p. 199-200° (decomp.). The ethereal filtrate was freed of ether and phenylethylamine in vacuo and the oily residue was dried over phosphorus pentoxide. Prolonged trituration in dry ether yielded another 2-4 g product. Two recrystallizations of the total product from 50% aqueous alcohol gave 18 g (53%), m. p. 201-202° (with decomp.). R_f 0.96 (same chromatographic conditions as in preceding experiment).

Found %: C 63.44; H 7.81; N 10.59. $C_{14}H_{20}O_3N_2$. Calculated %: C 63.60; H 7.65; N 10.60.

Hydrochloride. 2.6 g N-phenylethyl-β-isopropylidene-aminohydroxypropionic acid was suspended in 10 ml anhydrous methanol, and a solution of hydrogen chloride in methanol was added dropwise until the precipitate dissolved. The transparent solution was evaporated to dryness; the residual oil was triturated with ether (the solvent was replaced by a fresh portion up to 20 times) to form a white, hygroscopic solid which was recrystallized from dry acetone. Yield 2.5 g (85%), m. p. 159-160°.

Found %: Cl 12.08; N 8.98. $C_{14}H_{21}O_3N_2Cl$. Calculated %: Cl 11.81; N 9.31.

α-Benzylamino-β-isopropylidene-aminohydroxypropionic acid. A mixture of 18 g α-chloro-β-isopropylidene-aminohydroxypropionic acid and 53.5 g freshly distilled benzylamine was heated 8.5 hour on a boiling water bath. After cooling, addition was made of 200 ml ether. The precipitate was filtered, washed with ether, dissolved in the minimum quantity of hot water and again filtered. After standing 6-8 days at 5-10°, the filtrate deposited crystals which were filtered and washed with cold alcohol and ether. Yield 1-3 g α-benzyl-β-isopropylidene-aminohydroxypropionic acid with m. p. 178-179° (decomp.). The ethereal filtrate was worked up as in the preceding experiment to give an additional crop of 10-13 g of product with m. p. 176-178° (decomp.). Total yield of aminoacid 13-14 g (50%). R_f 0.91 (chromatographic condition as above).

Found %: C 62.65; H 7.13; N 10.91. $C_{13}H_{18}O_3N_2$. Calculated %: C 62.41; H 7.19; N 11.20.

Hydrochloride. 2.5 g N-benzyl-β-isopropylidene-aminohydroxypropionic acid was suspended in 20 ml anhydrous methanol, and dry hydrogen chloride was passed through until the solid had dissolved. The transparent solution was evaporated to dryness, the residue was dissolved in the minimum quantity of warm dichlorethane, and hot toluene was added dropwise until the liquid was turbid. The mass was then cooled to 5° and the hygroscopic precipitate was quickly filtered and dried at 50° over paraffin wax and alkali. Yield 2.4 g hydrochloride (80%), m. p. 114-115°.

Found %: Cl 12.71. $C_{13}H_{19}O_3N_2Cl$. Calculated %: Cl 12.36.

α-Piperidyl-β-isopropylidene-aminohydroxypropionic acid. To 15.5 g α-chloro-β-isopropylidene-aminohydroxypropionic acid, cooled with a mixture of dry ice and acetone, was added 37 g freshly distilled piperidine. After 30 minutes the cooling was stopped and the reaction mixture was stirred. It was then heated 5 hr on a boiling water bath. 100 ml ether was added and the precipitated piperidine hydrochloride was filtered, washed with ether and dried. The ether and piperidine were distilled off from the etheral filtrate in vacuo; the oily residue, dried over phosphorus pentoxide, was dissolved in the minimum quantity of absolute ether and stood 3-4 days at 5°. The liquid was triturated with dry ligroine (added dropwise) until faint turbidity appeared. It was then stood 2-3 days at room temperature. The precipitate was then filtered and washed with absolute ether. Yield of α-piperidyl-β-isopropylidene-aminohydroxypropionic acid 7.5-8 g (36-38%), m. p. 156-160° (with decomp.). Recrystallization from the minimum quantity of dioxane gave 3.7 g (19%) α-piperidyl-β-isopropylidene-aminohydroxypropionic acid with m.p. 163-165° (decomp.). R_f 0.86 (chromatographic conditions as above).

Found %: C 57.90; H 8.71; N 12.18. $C_{11}H_{20}O_3N_2$. Calculated %: C 57.91; H 8.77; N 12.28.

Preparation of Analogs of Cycloserine (IV)

4-Methylamino-3-isoxazolidone. 5 g α-methylamino-β-isopropylidene-aminohydroxypropionic acid was dissolved in a mixture of 24 ml conc. HCl and 24 ml methanol, and the reaction mixture was boiled in a flask joined to a column. The slowly distilling acetone was collected. The reaction mixture was evaporated to dryness in vacuo and the residue was dissolved with heating in 100 ml anhydrous ethanol. 50 ml of the solvent

was then distilled off. The warm solution was transferred to a flask fitted with a reflux condenser and a gas inlet tube. It was saturated with hydrogen chloride while being heated on an oil bath at 115-120°. When saturation was complete, the mass was boiled 1.5 hr and then left overnight. The ammonium chloride was then filtered off, the filtrate was evaporated to dryness in vacuo, and the residue was crystallized from anhydrous isopropyl alcohol. Yield 3.6 g (54%) of the dihydrochloride of ethyl α-methylamino-β-aminohydroxypropionate with m. p. 148-150°.

Found %: Cl 30.18. $C_6H_{16}O_3N_2Cl_2$. Calculated %: Cl 30.15.

1.5 g of the dihydrochloride was dissolved by heating in the minimum quantity of anhydrous methanol; 6 ml 2 N solution of potassium hydroxide in methanol was stirred in, the mixture was cooled, and the potassium chloride was separated. The filtrate was boiled 3 minutes, cooled and acidified with acetic acid to pH 5.5-6. After an hour the precipitate was filtered and washed with cold methanol and ether. Yield of 4-methylamino-3-isoxazolidone 0.45 g (60%), m. p. 147-148° (decomp.). Characteristic blue coloration with aqueous sodium nitroprusside. R_f 0.28 [ascending chromatogram; Whatman No. 1; mobile phase: tert-butanol–n-butanol–1 N aqueous NH_4OH (1:1:5), 12 hr, development with 4% aqueous sodium nitroprusside solution].

Found %: C 41.59; H 7.05; N 23.08. $C_4H_8O_2N_2$. Calculated %: C 41.37; H 6.94; N 24.12.

4-Phenylethylamino-3-isoxazolidone. 5.0 g α-phenylethylamino-β-isopropylidene-aminohydroxypropionic acid was dissolved in 20 ml conc. HCl, 20 ml methanol was added, and the mixture was refluxed 2-2.5 hr on an oil bath at 115-120°. The mixture was evaporated to dryness in vacuo, and the residue was dissolved by heating in 50 ml anhydrous methanol. The solution was transferred to a flask fitted with a reflux condenser and a gas inlet tube. A stream of dry hydrogen chloride was passed for 2 hr through the heated mixture. The following day the methanol was distilled off in vacuo, 50 ml dry methanol was added to the residue, and the reaction mixture was agina evaporated to dryness in vacuo. The resulting oily dihydrochloride of the methyl ester of α-phenethylamino-β-aminohydroxypropionic acid was dissolved in 30 ml 2 N alcoholic potassium hydroxide, and the reaction mixture was boiled 3-5 min on a water bath, cooled, and filtered from the potassium chloride. Acetic acid was added to the filtrate to a pH of 7.5-8 and the liquid was concentrated in vacuo at a bath temperature of 20-25°. The residue was dissolved in 15 ml water, the pH of the solution was brought to 7-6.5, the oily layer was separated, and the solution was acidified with dilute acetic acid to a pH of 5-5.5; crystallization of 4-phenylethylamino-3-isoxazolidone then commenced and was complete in 24 hr. Yield 0.45 g (11.5% reckoned on the aminoacid); m. p. 146-147° (with decomp.).

Found %: 13.86; C 63.85; H 6.80. $C_{11}H_{14}O_2N_2$. Calculated %: N 13.61; C 64.06; H 6.84.

4-Benzylamino-3-isoxazolidone. 2.5 g α-benzylamino-β-isopropylidene-aminohydroxypropionic acid was dissolved in 10 ml conc. HCl and 10 ml methanol was added. The mixture was boiled 2 hr at 115-120° and evaporated to dryness in vacuo; the residue was dissolved in 40 ml anhydrous methanol and the resulting transparent solution was again boiled 2 hr while a continuous stream of dry hydrogen chloride was introduced. The next day the methanol was taken off in vacuo, the traces of hydrogen chloride were removed, and the dihydrochloride of the methyl ester of α-benzylamino-β-aminohydroxypropionic acid was cyclized by treatment with 15 ml 2 N alcoholic potassium hydroxide. The product was worked up as in the preceding experiment. Yield 0.2 g (10% reckoned on the aminoacid), m. p. 150-151°. Characteristic blue coloration with aqueous sodium nitroprusside. R_f 0.56 (chromatographic conditions as above).

Found %: N 14.60. $C_{10}H_{12}O_2N_2$. Calculated %: N 14.61.

Attempt to prepare 4-piperidyl-3-oxazolidone. 2.3 g α-piperidyl-β-isopropylidene-aminohydroxypropionic acid was dissolved in a mixture of 10 ml conc. HCl and 10 ml methanol, and the mixture was boiled 3 hr at 120°. The resulting transparent solution was evaporated to dryness and the residue treated several times with anhydrous acetone. The precipitated piperidine hydrochloride was filtered off and washed with ether (0.6 g, 50%), m. p. 237°. A mixture with authentic piperidine hydrochloride did not suffer a depression of melting point.

The filtrate was evaporated to dryness, dissolved in 25 ml anhydrous ethanol and esterified in the usual manner. After the solvent had been driven off, the residual oil was treated with 10 ml 2 N methanolic potassium hydroxide as described above. A specimen of the solution was chromatogrammed on Whatman no. 1 for 12 hr with a mobile phase comprisong tert-butanol–n-butanol–1 N aqueous NH_4OH (1:1:5). Drying followed

by development with 4% aqueous sodium nitroprusside gave the characteristic blue trace of piperidyl-3-oxazo-lidone; $R_f = 0.47$. 4-Piperidyl-3-oxazolidone could not be isolated in crystalline form.

Deamination of α-piperidyl-β-isopropylidene-aminohydroxypropionic acid hydrochloride. To a sus-pension of 2.28 g α-piperidyl-β- isopropylidene-aminohydroxypropionic acid in 10 ml butyl alcohol was added the equivalent quantity of conc. HCl. After the solid had dissolved, 2-3 drops 36% hydrochloric acid was added and the mixture was refluxed 8 hr at an oil bath temperature of 150-160°. The resulting colorless solution gave a characteristic red coloration with an alkaline solution of sodium nitroprusside, indicating the presence of pyruvic acid in solution. The solution was evaporated to dryness, the residue was treated with 10 ml dry acetone, and the precipitate was filtered off, washed with ether and dried. Yield 0.45 g (38%) of piperidine hydrochloride with m. p. 237-240°. No depression in mixed melting point test with an authentic specimen.

Phenylethylethyleneimino-2-carbohydroxamic acid. To a solution of 87.5 g freshly distilled methyl ester of α,β-dibromopropionic acid in 200 ml dry benzene was added at 5° a mixture of 71.4 g triethylamine and 43 g phenylethylamine in 350 ml dry benzene. The precipitate of triethylamine hydrobromide was filtered off, and the filtrate was boiled 3 hours on a water bath before being left for 24 hours at room temperature. The reaction mixture was then subjected to extraction with water; the benzene layer was collected, dried with mag-nesium sulfate and distilled in vacuo for removal of benzene. The residue was dissolved in 50 ml dry methanol and the solution gradually stirred at 5° into a solution prepared by mixing a suspension of 50 g hydroxylamine hydrochloride in 200 ml methanol with a solution of sodium methoxide (25 g sodium in 300 ml methanol). The reaction mixture was held for 24 hr at room temperature and filtered from the sodium chloride; the filtrate was evaporated in vacuo to a volume of 200-250 ml and diluted with 200 ml water. Gradual addition was then made (with cooling) of 65 ml glacial acetic acid. The precipitate was filtered, washed with water and recrystallized from alcohol. Yield of phenylethylethyleneimino-2-carbohydroxamic acid 43.5 g (60%), m. p. 148-150°.

Found %: N 13.59. $C_{11}H_{14}O_2N_2$. Calculated %: N 13.61.

α-Phenylethylamino-β-chloropropionohydroxamic acid hydrochloride. A stream of dry hydrogen chlo-ride was passed for 30 min, with stirring and cooling (iced water), into a suspension of 10.3 g phenylethyleth-yleneimino-2-carbohydroxamic acid in 100 ml dry benzene. Cooling was then stopped and hydrogen chloride was passed in for another 45-50 min. The next day the reaction mixture was diluted with 100 ml dry ether and filtered; the precipitate was washed with ether on the filter and dried in the air. Yield of mixture of hydro-chlorides of the isomeric haloamino-substituted hydroxamic acids 13.5 g (100%), m. p. 80-120°. The mixture was crystallized from anhydrous ethanol; the hydrochloride of α-phenylethylamino- β-chloropropionohydrox-amic acid was obtained; yield 6.2 g (46%), m. p. 161-163° (with decomp.).

Found %: Cl 12.70. $C_{11}H_{16}O_2N_2Cl_2$. Calculated %: Cl 12.71.

4-Phenylethylamino-3-isoxazolidone. 1.55 g α-phenylethylamino-β-chloropropionohydroxamic acid hydrochloride was gradually added to a warm solution of 1.1 g sodium bicarbonate in 10 ml water. The reac-tion mixture was boiled 2-3 min, cooled brought to pH 7-7.5 with acetic acid, and filtered. The filtrate was brought to pH 5.5-6 by dilution with acetic acid. After 24 hours the N-phenylethylcycloserine was filtered off; yield 0.4 g (40%), m. p. 146-147° (with decomp.). The product was identical with 3-phenylethylamino-3-oxazolidone obtained by another method.

4-Benzylamino-3-isoxazolidone. Addition was made portionwise, with stirring, of 3 g α-benzylamino-β-chloropropionohydroxamic acid hydrochloride to a hot solution of 2 g sodium bicarbonate in 15 ml water. The transparent solution was boiled 3-4 min and cooled. 10 ml alcohol was added and the pH of the medium brought to 7.5-6 (Bromthymol blue test). After filtration, the pH of the filtrate was brought to 5.5 and the liquid was kept in a refrigerator for 48 hours. The crystalline precipitate was filtered, washed with a little cold water and dried in a desiccator over phosphorus pentoxide. Yield of 4-benzylamino-3-isoxazolidone 1 g (50%). M. p. 150-152° (from alcohol). The product was fully identical with 4-benzylamino-3-isoxazolidone obtained by another route.

SUMMARY

1. The previously developed general method of synthesis of 4-amino-3-isoxazolidones was used for the synthesis of analogs of cycloserine containing a substituted amino group (4-methylamino-3-isoxazolidone, 4-benzylamino-3-oxazolidone and 4- β-phenylethylamino-3-oxazolidone).

2. It was shown that substitution in the amino group of cycloserine completely destroys the chemotherapeutic acitivity.

3. It was found that N-substituted derivatives of β-isopropylidene-aminohydroxypropionic acids undergo deamination in an acid medium, and a theory of the mechanism of this reaction is put forward.

4. The scheme proposed by other authors for cyclization of N-substituted β-chlorohydroxyaminopropionic acids to derivatives of 4-amino-3-isoxazolidones was improved.

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REACTIONS OF β-CHLOROVINYL KETONES WITH β-DICARBONYL COMPOUNDS

VIII. SYNTHESIS OF POLYSUBSTITUTED DERIVATIVES OF BENZENE. A NEW VARIANT OF THE DIENE SYNTHESIS

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In a preceding communication [1], we described the reaction of β-chlorovinyl ketones with ethylacetoacetate in presence of potassium carbonate, and it was shown that the reaction goes in more than one direction; in presence of a large excess of ethylacetoacetate the main product is the ethyl ester of a 4-alkylsalicylic acid. With a smaller excess of ethylacetoacetate the yield of ester of 4-alkylsalicylic acid falls off sharply. Reaction of methyl-β-chlorovinyl ketone with ethylacetoacetate enabled isolation in appreciable quantities of a crystalline compound with m. p. 61°. It was previously [1] suggested that this compound is a derivative of dihydrobenzofuran and is the result of further transformations of the initially formed product of bis-ketovinylation of ethylacetoacetate. We are inclined to the opinion that bis-ketovinylation (which is associated with transmethylation of the originally formed monoketovinylated ethylacetoacetate) is the main cause of the complications arising during ketovinylation of β-dicarbonyl compounds [1, 2].

In the present work, we elucidated the structure of the substance with m. p. 61° and of its analogs. The routes to its formation are discussed, and preparative applications of the results are described.

It was previously shown [1] that a smaller excess of ethylacetoacetate in its reaction with methyl β-chlorovinyl ketone in presence of potassium carbonate leads to a sharp drop in yield of the ester of 4-methylsalicylic acid, while the yield of substance with m. p. 61° gradually rises. Closer investigation showed that the yield of substance with m. p. 61° rises rapidly with increasing ratio of methyl β-chlorovinyl ketone to ethylacetoacetate and reaches a maximum when the ratio is 2 : 3. The quantity of solvent (benzene was the most convenient) also played an important part. Thus, the yield was 23% when the volume of benzene was 10 times that of the methyl β-chlorovinyl ketone; it was 51% when 6 volumes of solvent were present, 70% with 3 volumes of solvent, and 81% with 1½ volumes of solvent. The optimum yield of compound with m. p. 61° is therefore obtained by reaction of 2 moles methyl β-chlorovinyl ketone with 3 moles ethylacetoacetate in 1.5 times the volume of benzene in presence of calcined potassium carbonate. Under these conditions the substance with m. p. 61° is substantially the sole product of the reaction and is formed in a yield of about 80%, so that it is readily available for examination and further utilization.

The compound with m. p. 61° did not decolorize an aqueous or acetone solution of permanganate, was insoluble in aqueous solutions of caustic alkali or sodium carbonate, and did not give a coloration with aqueous ferric chloride. Consequently it does not contain a double bond or an enolic or phenolic hydroxyl. The analysis and molecular weight indicated the composition $C_{14}H_{16}O_4$. Halogen is absent. Its empirical formula could result from reaction of 2 moles methyl β-chlorovinyl ketone with 1 mole ethylacetoacetate to give 1 mole water and 2 moles hydrogen chloride.

$$C_6H_{10}O_3 + 2C_4H_5OCl \rightarrow C_{14}H_{16}O_4 + H_2O + 2HCl$$

It gave a mono-dinitrophenylhydrazone $C_{20}H_{20}O_7N_4$ and a positive reaction for iodoform. This indicated the presence of one acetyl group. Saponification of the substance with aqueous-alcoholic sodium hydroxide gave a monobasic acid $C_{12}H_{12}O_4$, which was decarboxylated by heating in quinoline in presence of copper chromite and gave a crystalline substance with m. p. 35.5° and the empirical formula $C_{11}H_{12}O_2$. The latter likewise formed a mono-dinitrophenylhydrazine. This points to the presence of one carbethoxy group in the compound with m. p. 61°.

Oxidation with excess of potassium permanganate in an alkaline medium gave an aromatic polycarboxylic acid with m. p. 237-238° whose analysis (as well as the analysis of its barium salt) indicated that it is a benzene tetracarboxylic acid. Its melting point was the same as that of benzene-1,2,3,5-tetracarboxylic acid. The tetracarboxylic acid was dehydrated by heating at 250-260° and the resulting anhydride was sublimed in vacuo. Analysis of the latter enabled it to be identified as the monoanhydride of the benzene-tetracarboxylic acid. Formation of a dianhydride could not be observed even after more prolonged and also after repeated heating. These data, in conjunction with the melting point (238°), indicated that the anhydride was the monoanhydride of benzene-1,2,3,5-tetracarboxylic acid. The two other isomeric acids — benzene-1,2,3,4-tetracarboxylic and benzene-1,2,4,5-tetracarboxylic acid — would naturally have formed dianhydrides under our conditions.

Exhaustive oxidation of the compound with m. p. 61° thus leads to benzene-1,2,3,5-tetracarboxylic acid and demonstrates that the compound is a benzene derivative containing four substituents in the 1,2,3 and 5 positions. We oxidized the substance with concentrated nitric acid at 150-160° with the objective of obtaining further evidence of its structure. From the products of this reaction was isolated a tribasic acid which was identified as methytrimesic acid. Hence, one of the substituents in the compound with m. p. 61° is a methyl group.
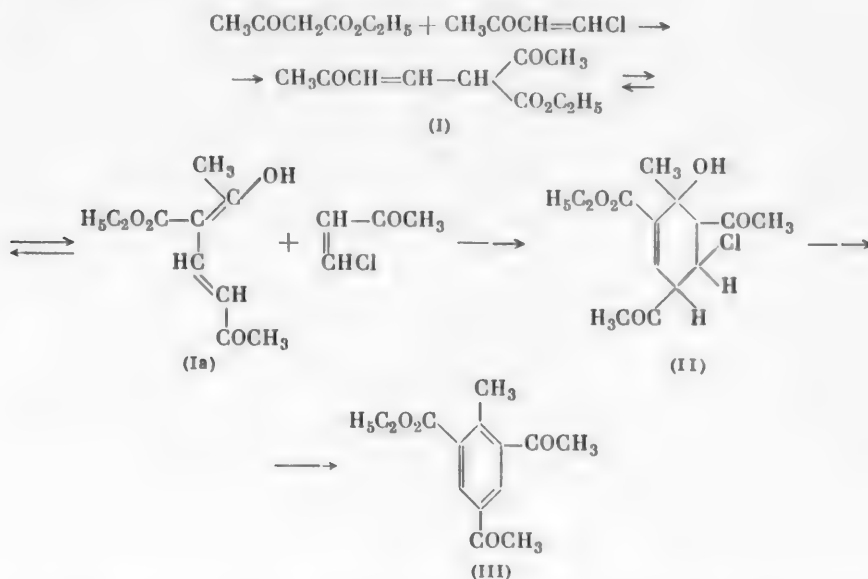
It is clear from the results of saponification and oxidation that the compound contains acetyl, carbethoxyl and methyl groups in the 1, 2, 3 and 5 positions. The nature of the fourth substituent follows from consideration of the empirical formula, which shows that it must be also an acetyl group. The compound with m. p. 61° is therefore the ethyl ester of a methyldiacetylbenzoic acid. The relative positions of the methyl, carethoxyl, and acetyl groups are established by consideration of the paths of formation of the compound (see below): the compound is the ethyl ester of 2-methyl-3,5-diacetylbenzoic acid.

The above reactions, which led to clarification of the structure, are represented by the following scheme:
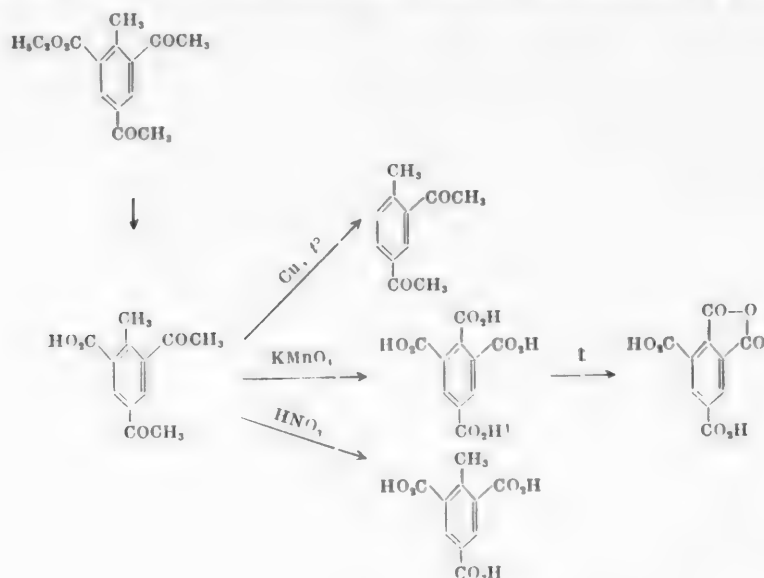
Formation of the ethyl ester of 2-methyl-3,5-diacetylbenzoic acid on condensation of methyl β-chlorovinyl ketone with ethylacetoacetate is a somewhat unusual reaction. In the first step (in presence of potassium carbonate) the methyl-β-chlorovinyl ketone apparently ketovinylates the ethylacetoacetate by the general

mechanism (compare [2, 3]) to form α-(γ-ketobutenyl)-acetoacetic ester (I). The latter can be cyclized to the ester of 4-methylsalicylic acid when there is a large excess of acetoacetic ester [1]. On the other hand, with a large proportion of methyl-β-chlorovinyl ketone (as in our case) (I) enters into reaction with a second molecule of the β-chlorovinyl ketone by a dienic mechanism, (I) functioning in the enolic form (Ia). The resulting unstable intermediate adduct (II) loses a molecule of water and hydrogen chloride to form the aromatic system — the ester of 2-methyl-3,5-diacetylbenzoic acid (III).

$$CH_3COCH_2CO_2C_2H_5 + CH_3COCH=CHCl \longrightarrow$$

$$\longrightarrow CH_3COCH=CH-CH{\overset{COCH_3}{\underset{CO_2C_2H_5}{}}} \rightleftharpoons$$

(I)

(Ia)   (II)   (III)

In the diene synthesis step, another orientation of the diene (Ia) with respect to methyl β-chlorovinyl ketone would be possible. This would lead, however, to a 1,2,4,5-tetrasubstituted benzene derivative, and we have seen that oxidation of the reaction product gives not 1,2,4,5- but 1,2,3,5-benzenetetracarboxylic acid.

No objections can be raised to the proposed scheme since the dienophilic activity of β-chlorovinyl ketones is well known [3-5] and the susceptibility to enolization of γ-ketobutenylacetoacetic ester (I) must be intensified (in comparion with acetoacetic ester itself), the carbonyl of the acetyl group being under more favorable conditions for enolization than the carbonyl of the ketovinyl group.

The only unusual feature (and also the most interesting one) in the proposed scheme is the functioning of the enol form of a carbonyl compound as a diene. This type of diene had not previously been encountered in diene syntheses. Only when this work had been completed did a paper appear by Braude [6] in which the enolic form of mesityl oxide was postulated as a dienic component in order to account for the dimerization of mesityl oxide under the action of metallic lithium. In our case, the progress of the reaction is greatly facilatated by the subsequent aromatization of the adduct with formation of a stable compound. Still obscure is the role of the potassium carbonate in the second step — dienic condensation. One possibility is that potassium carbonate facilitates enolization of (I); it may also lead to formation of a metal enolate which also undergoes dienic condensation.

Formation of ethyl 2-methyl-3,5-diacetylbenzoate during condensation of ethylacetoacetate with methyl β-chlorovinyl ketone is consequently an entirely new type of reaction of β-chlorovinyl ketones. The two most important characteristics of the reactivity of this group of ketones are manifested in the reaction — the susceptibility to ketovinylation and the dienophilic activity.

The results obtained are important also for the understanding of the complications that arise during the ketovinylation of β-dicarbonyl compounds which we are now studying [1-3]. It is now clear that we must also reckon with the dienophilic activity of the monoketovinylated products of the reaction since the data leave no doubt about the reality of this activity. On the question of the process of bis-ketovinylation [1, 2, 7], this is

still unclarified, since we have no direct experimental evidence either in refutation of this possibility or in adequate support of it.

The above results also open out a new route (convenient for preparative work) to what were difficultly accessible and almost unknown derivatives of benzene, since under our chosen conditions the ethyl ester of 2-methyl-3,5-diacetylbenzoic acid is obtained in very high yield.

We have therefore made a closer study of the reaction in order to establish its applicability to other β-chlorovinyl ketones and other β-dicarbonyl compounds. Under the same conditions (in presence of calcined potassium carbonate in boiling benzene) other β-chlorovinyl ketones (phenyl β-chlorovinyl ketone and p-chloro-phenyl β-chlorovinyl ketone)also condense with ethylacetoacetate to give high yields of the esters of the corresponding 2-methyl-3,5-diacylbenzoic acids.

$$CH_3COCH_2CO_2C_2H_5 + 2RCOCH{=}CHCl \longrightarrow$$

$$R = C_6H_5, \quad p\text{-}ClC_6H_4.$$
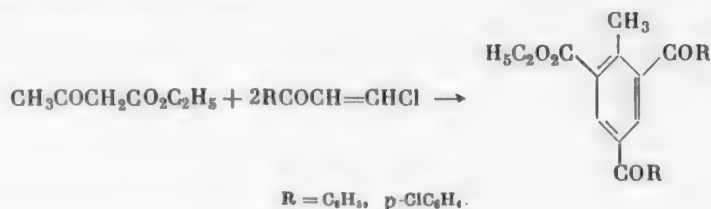
It was also found that not only ethylacetoacetate but also β-diketones enter into this reaction. For example, acetylacetone condenses with methyl β-chlorovinyl ketone under the above-described conditions (i.e., with heating with calcined potassium carbonate in boiling toluene) to give 2,4,6-triacetyltoluene in a yield exceeding 60%. The structure of the product was confirmed by its exhaustive oxidation with potassium permanganate, which led to benzene-1,2,3,5-tetracarboxylic acid.

$$2CH_3COCH{=}CHCl + CH_3COCH_2COCH_3 \longrightarrow \xrightarrow{KMnO_4}$$
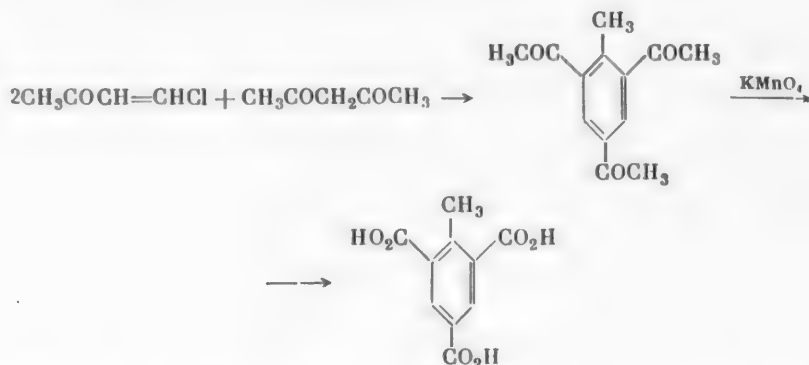
It is quite obvious that condensation of β-chlorovinyl ketones with acetylacetone follows the same route and likewise leads to a tetrasubstituted benzene derivative which is not easily accessible by any other route.

The data presented in this paper show that the characteristic condensation of β-chlorovinyl ketones with β-dicarbonyl compounds in presence of potassium carbonate is fairly general in character. Apart from the fundamental interest of the ability of unsaturated dicarbonyl compounds to enter into dienic reactions with dienophilic compounds, this reaction is unquestionably of preparative interest in providing a route to difficultly accessible polysubstituted derivatives of benzene.

EXPERIMENTAL

Ethyl 2-methyl-3,5-diacetylbenzoate. In the course of an hour 133 g (1.3 moles) methyl β-chlorovinyl ketone was added to a mixture of 260 g (2 moles) ethylacetoacetate and 276 g (2 moles) calcined potassium carbonate in 180 ml dry benzene. After heat had ceased to be released, the vigorously stirred reaction mass was boiled 4 hr; after cooling, 250 ml water was added, the benzene layer was separated, the aqueous layer

was extracted with ether, and the combined ether-benzene extracts were dried with magnesium sulfate. The solvents were boiled off and the residue distilled in vacuo. The 160-165° (1 mm) fraction was collected. The yield of ethyl 2-methyl-3,5-diacetylbenzoate was 120.5 g (81%). Introduction of a seed crystal led to complete crystallization. M. p. 61° (from a mixture of benzene and ligroine, and then from methanol). Colorless crystals, insoluble in water and ligroine, readily soluble in alcohol and benzene.

Found %: C 68.05, 67.97; H 6.57, 6.52. M (after Rast.) 258.2, 245.2. $C_{14}H_{16}O_4$. Calculated %: C 67.76; H 6.49. M 248.3.

Dinitrophenylhydrazone. Prepared in the usual manner; m. p. 175° (from dilute acetic acid).

Found %: N 13.32. $C_{20}H_{20}O_7N_4$. Calculated %: N 13.38.

2-Methyl-3,5-diacetylbenzoic acid. 21 g ethyl 2-methyl-3,5-diacetylbenzoate was boiled 30 min with an aqueous alcoholic solution of NaOH, 12.6 g of NaOH, 73 ml alcohol, 42 ml water). After cooling, the mass was treated with hydrochloric acid until neutral to litmus, the alcohol was distilled off in vacuo, and 50 ml water was added, followed by acid until mass had an acid reaction. The resulting crystals were filtered and dried in vacuo; yield 17.7 g (95%), m. p. 141° (from toluene). Colorless, fine crystals, insoluble in water, soluble in alcohol, ether, acetone, aqueous sodium hydroxide and sodium carbonate.

Found %: C 65.52, 65.77; H 5.75, 5.74. $C_{12}H_{12}O_4$. Calculated %: C 65.45; H 5.49.

2,4-Diacetyltoluene. 4 g 2-methyl-3,5-diacetylbenzoic acid was heated 1 hr at 250-260° with 4 g copper chromite in 40 ml freshly distilled quinoline. The catalyst was filtered off, the mass was poured into 300 ml 10% hydrochloric acid, and the reaction product was extracted with ether. The ethereal extracts were washed with water and sodium carbonate and dried; the ether was driven off, and the residue distilled in vacuo. The 144-146° (7 mm) fraction was collected. Yield 2.2 g (72.6%). The compound crystallized completely and had m.p. 35-35.5°.

Found %: C 74.70; H 7.12. $C_{11}H_{12}O_2$. Calculated %: C 75.00; H 6.82.

Dinitrophenylhydrazone. Prepared in the usual manner; m. p. 210° (from alcohol).

Found %: C 57.40, 57.21. H 4.62, 4.64; N 15.23, 15.41. $C_{17}H_{16}O_5N_4$. Calculated %: C 57.30; H 4.50; N 15.70.

Oxidation of 2-methyl-3,5-diacetylbenzoic acid with potassium permanganate. 61 g pulverized potassium permanganate was added in small portions with stirring and cooling to a solution of 11 g 2-methyl-3,5-diacetylbenzoic acid in 80 ml 10% sodium hydroxide. The reaction mass was thereupon boiled 2 hours. After cooling, the excess of potassium permanganate was destroyed with acetone. After filtration, the precipitate was washed with hot water, the combined filtrates were neutralized with hydrochloric acid, and 120 ml saturated barium chloride solution was added. The precipitate of barium salt of benzene-1,2,3,5-tetracarboxylic acid was filtered, washed with distilled water and dried in vacuo over phosphorus pentoxide.

Found %: Ba 52.07. $C_{10}H_2O_8Ba_2$. Calculated %: Ba 52.30.

The barium salt was dissolved in the minimum quantity of 3 N HCl, the solution was filtered, and 10% H_2SO_4 solution was added dropwise until a precipitate ceased to be formed. The barium sulfate was filtered off and the aqueous solution was evaporated until crystallization commenced. After cooling, the precipitate was filtered and dried 2 hr at 110°. Yield 9.6 g (74%), m. p. 237-238° (from hydrochloric acid). The literature [8] gives m. p. 238°.

Found %: C 47.47, 47.61; H 2.65, 2.52. $C_{10}H_6O_8$. Calculated %: C 47.24; H 2.36.

Benzene-1,2,3,5-tetracarboxylic anhydride. 1 g of the prepared acid was held for an hour at 250-270°. After cooling, the melt was pulverized and sublimed in vacuo. Yield of anhydride 0.74 g (80%), m. p. 238°.* The literature [9] gives m. p. 238°.

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*The melting point of the anhydride is the same as that of the original acid; this is quite evidently due to anhydride formation from the acid before melting, so that the substance that melts is the anhydride.

Found %: C 51.41, 51.31; H 2.25, 2.32. $C_{10}H_4O_7$. Calculated %: C 50.86; H 1.71.

Oxidation of 2-methyl-3,5-diacetylbenzoic acid with nitric acid. 1 g 2-methyl-3,5-diacetylbenzoic acid was boiled 6 hours with 3 ml nitric acid (d 1.52) and 1 ml water. Another 1 ml nitric acid was then added before boiling of the mass 2.5 hours. The resulting crystals of methyltrimesic acid were filtered, dried in vacuo, and finally dried in a cupboard at 110-120°. M. p. 308-309° (with decomp.). The literature [10] reports m.p. 309-310°.

Found %: C 53.19, 53.26; H 3.56, 3.55. $C_{10}H_8O_6$. Calculated %: C 53.57; H 3.57.

Ethyl 2-methyl-3,5-dibenzoylbenzoate. Prepared similarly to ethyl 2-methyl-3,5-diacetylbenzoate from 16.1 g phenyl β-chlorovinyl ketone, 20 g ethylacetoacetate, 30 g potassium carbonate in 30 ml dry benzene. The crystalline mass remaining after the solvent had been driven off was recrystallized from aqueous alcohol. Yield 14.3 g (85%), m. p. 104°. Colorless crystals, insoluble in water, easily soluble in alcohol and benzene.

Found %: C 77.79, 77.58; H 5.51, 5.52. $C_{24}H_{20}O_4$. Calculated %: C 77.40; H 5.41.

Ethyl ester of 2-methyl-3,5-di-(p-chlorobenzoyl)-benzoic acid. Prepared similarly to preceding compound from 13 g p-chlorophenyl β-chlorovinyl ketone, 26 g ethylacetoacetate, 26 g potassium carbonate in 50 ml anhydrous benzene. Yield 8.2 g (58%), m. p. 110° (from aqueous alcohol). Colorless crystals, insoluble in water, readily soluble in organic solvents.

Found %: Cl 16.24, 16.59. $C_{24}H_{18}O_4Cl_2$. Calculated %: Cl 16.10.

2,4,6-Triacetyltoluene. Prepared similarly to the last compound from 29 g methyl β-chlorovinyl ketone, 45 g acetylacetone and 45 g calcined potassium carbonate. The crystalline mass remaining after the solvent had been driven off from the extracts was recrystallized from aqueous alcohol.

Yield 19.5 g (63%), m. p. 73°. Colorless acicular crystals, insoluble in water, readily soluble in organic solvents.

Found %: C 71.42, 71.42; H 6.47, 6.54. $C_{13}H_{14}O_3$. Calculated %: C 71.56; H 6.42.

Oxidation of 2,4,6-triacetyltoluene. The oxidation procedure was similar to that for the oxidation of 2-methyl-3,5-diacetylbenzoic acid, using 25 ml 2 N potassium hydroxide solution and 49 g potassium permanganate for 4.4 g 2,4,6-triacetyltoluene. Yield of benzene-1,2,3,5-tetracarboxylic acid 1.6 g (35%), m. p. 238°. A mixture of with benzene-1,2,3,5-tetracarboxylic acid prepared in preceding experiments did not suffer a depression of melting point.

SUMMARY

1. It was shown that condensation of 2 moles methyl β-chlorovinyl ketone with 1 mole ethylacetoacetate in presence of potassium carbonate gives the ethyl ester of 2-methyl-3,5-diacetylbenzoic acid.

2. A mechanism is proposed for the formation of this compound whereby in a first step the product of monoketovinylation enters in its enol form into dienic synthesis with a second molecule of the β-chlorovinyl ketone. It was thus shown for the first time that unsaturated dicarbonyl compounds are capable of functioning as dienes in the diene synthesis.

3. This reaction is shown to be widely applicable. It is undergone by various β-chlorovinyl ketones as well as by β-diketones. It is of preparative value for the synthesis of various polysubstituted benzene derivatives.

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PYRAZOLES

II. SYNTHESIS OF N-PHENYLPYRAZOLES FROM THE CORRESPONDING PYRAZOLINES

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In the preceding communication [2], we showed that pyrazolines with a free NH group are dehydrogenated to the corresponding pyrazoles when heated with sulfur.

In the present work we demonstrated the suitability of this method also for the dehydrogenation of N-phenyl-pyrazolines.

We prepared the starting N-phenylpyrazolines by cyclization of α,β-unsaturated carbonyl compounds or of Mannich bases with phenylhydrazine. The phenylhydrazone formed by interaction of phenylhydrazine with α,β-unsaturated ketones is immediately cyclized during the reaction under relatively mild conditions (80°, 1-2 hr), and the yields of pyrazoline are nearly quantitative. Complications arise, however, when an α,β-unsaturated aldehyde is reacted. Heating of phenylhydrazine for 30 hr at 85-90° with cinnamaldehyde led to a phenylhydrazone which cyclized only after 2-hours boiling with excess of glacial acetic acid. In the case of acrolein, we obtained a yield of only 30% when the phenylhydrazone was cyclized to N-phenylpyrazoline. These results are in line with the observations of Auwers [2-4] on the resistance of the phenyldrazones of α,β-unsaturated aldehydes to cyclization to pyrazolines.

We cyclized Mannich bases with phenylhydrazine by the general procedure. This involved boiling of β-dimethylaminoketones in aqueous solution with an equimolar quantity of phenylhydrazine hydrochloride followed by extraction of the N-phenylpyrazoline (which separated after 3-5 hr) with ether (yields 60-80%). All of the N-phenylpyrazolines that we prepared were dehydrogenated under the same conditions (180-220°, 1-2 hr) were used for pyrazolines with an unsubstituted NH group [1]. Yields of N-phenylpyrazolines were between 60 and 90%. Dehydrogenation with sulfur is therefore not associated with initial oxidation at the expense of the hydrogen of the NH group.

In addition to work on 1-phenylhydrazones with alkyl or phenyl substituents in the 3 or 5 position of the pyrazoline ring, we also dehydrogenated 1-phenyl-3-acetaminopyrazoline [6]. Under the usual conditions it gives 1-phenyl-3-acetaminopyrazole in a yield of over 85%. When the amino group is unsubstituted the reaction course is evidently more complicated, and 1-phenyl-3-aminopyrazole could be obtained in a yield of only 39%. The complexity of the reaction between primary amines and sulfur is attested by numerous publications (for example [7]).

The method here proposed has the advantage that pure N-phenylpyrazoles are formed. The usual method of synthesis of N-phenylpyrazoles from unsymmetrical β-diketones and substituted hydrazines leads to a mixture of N-substituted pyrazoles.

The pyrazoles obtained in the present and the preceding [1] work were analyzed for their ultraviolet absorption spectra*. All of the investigated pyrazoles with a free NH group and alkyl substituents possess an absorption band in the 225-210 mμ region (log ϵ 3.5) in agreement with the literature [8].

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*Absorption spectra were plotted with the SF-4 spectrophotometer. Methyl alcohol was the solvent in each case.

Introduction of a phenyl or furyl group into any position in the ring (1, 3, 4 or 5) causes the absorption band to be appreciably shifted in the direction of longer waves (by 20-23 mμ) to the 249-258 mμ region (log ε 4.3). 1,3-Diphenylpyrazole is an exception with λ_{max} 278 mμ. With an amino or acetamino group in the 3 position, the absorption band is in the 275-285 mμ region (log ε 4.3).
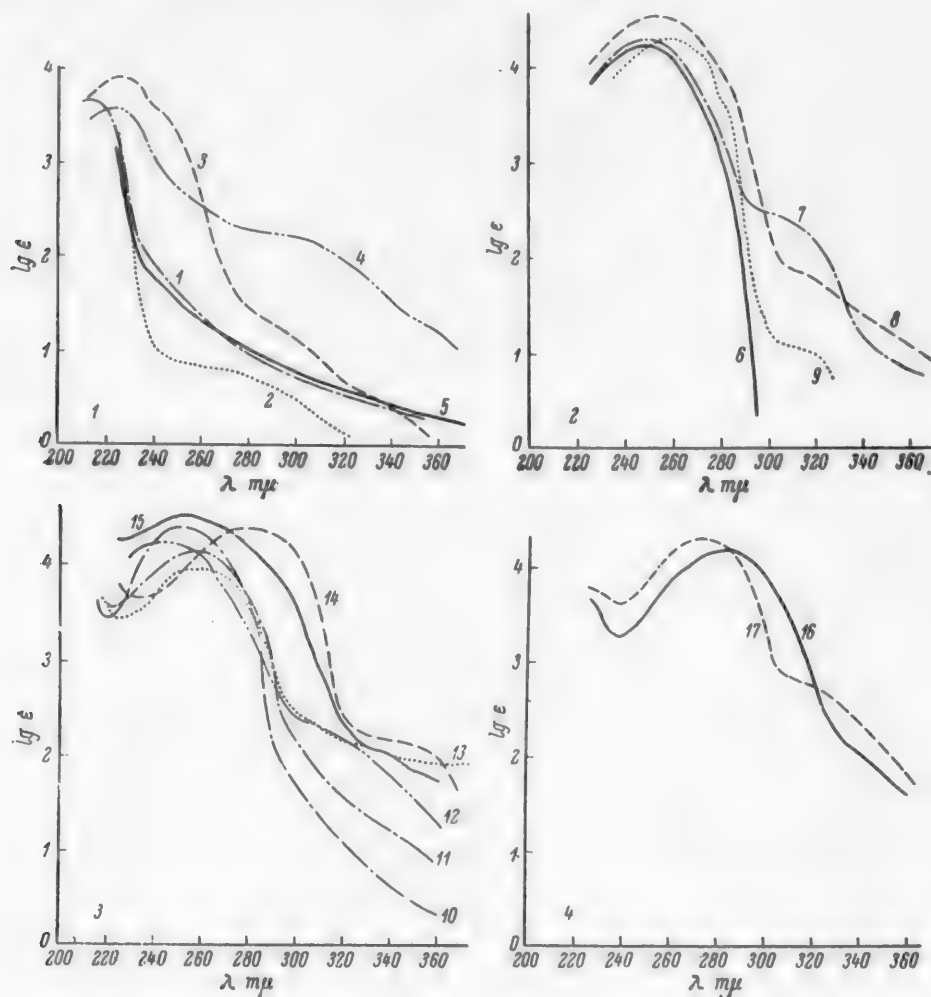
Ultraviolet absorption spectra of substituted pyrazoles. 1) 3-Methylpyrazole; 2) 3,5-dimethylpyrazole; 3) 4-ethyl-5-propylpyrazole; 4) 4-isopropyl-5-isobutylpyrazole; 5) 3-tert butylpyrazole; 6) 5-phenylpyrazole; 7) 3-methyl-5-phenylpyrazole; 8) 3,5-diphenylpyrazole; 9) 3-methyl-5-(2-furyl)-pyrazole; 10) 1-phenylpyrazole; 11) 1-phenyl-3-methylpyrazole; 12) 1,5-diphenylpyrazole; 13) 1-phenyl-3-tert-butylpyrazole; 14) 1,3-diphenylpyrazole; 15) 1,3,5-triphenylpyrazole; 16) 3-amino-1-phenylpyrazole; 17) 3-acetamino-1-phenylpyrazole.

Absorption curves are shown in the drawing and values of λ_{max} and log ε in the table.

EXPERIMENTAL

1-Phenylpyrazole. 400 ml ether was placed in a four-necked flask fitted with a stirrer, two dropping funnels and a reflux condenser. From the dropping funnels were simultaneous introduced (dropwise) 58 g acrolein and 108 g phenylhydrazine at such rates that addition of both of the components was completed after about

1.5 hr. It was necessary to maintain a temperature of the reaction mixture of not higher than 5-10°. After 5 hr the ether was driven off and the residue was transferred to a flask for distillation in steam to which 300 ml 2 N sulfuric acid was added. The N-phenylpyrazoline was distilled with steam. The pyrazoline was extracted from the distillate with ether, and the extract was dried with magnesium sulfate and distilled in vacuo to give 44 g (30%) N-phenylpyrazoline.

B. p. 143-146° (14 mm), $n^{20}D$ 1.6156, d^{20}_4 1.0984 [9], MR_D 46.48; calc. 43.84, EMR_D + 2.64.

Maxima of the Absorption Spectra of Substituted Pyrazoles in the Ultraviolet

Compound no.	Substituents and their position	λ_{max} (mμ)	lg ε
1	3-Methyl	<220	<3.5
2	3,5-Dimethyl	<220	>3.5
3	4-Ethyl-5-propyl	223	3.744
4	4-Isopropyl-5-isobutyl	224	3.607
5	3-Tert -butyl	<220	>3.2
6	3-Phenyl	249	4.243
7	3-Methyl-5-phenyl	251	4.285
8	3,5-Diphenyl	254	4.564
9	3-Methyl-5-(2-furyl)	258	4.283
10	1-Phenyl	251	4.408
11	1-Phenyl-3-methyl	256	4.146
12	1,5-Diphenyl	246	4.255
13	1-Phenyl-3-tert -butyl	257	3.995
14	1,3-Diphenyl	278	4.394
15	1,3,5-Triphenyl	252	4.537
16	3-Amino-1-phenyl	284	4.227
17	3-Acetamino-1-phenyl	274	4.330

29.2 g N-phenylpyrazoline was heated with 6.4 g sulfur to a gentle boil in a nitrogen stream in a 50-ml Claisen flask. Hydrogen sulfide ceased to come off after about an hour, and the reaction mixture was then distilled in vacuo to give 21.9 g (76%) 1-phenylpyrazole.

B. p. 106-109° (6 mm), 124° (10 mm), 141-142° (30 mm), $n^{20}D$ 1.5976, d^{20}_4 1.0908, MR_D 45.09; calc. 43.37, EMR_D + 1.72, m. p. 13° [10].
Found %: N 19.54, 19.57. $C_9H_8N_2$. Calculated %: N 19.43.

1-Phenyl-3-methylpyrazole. 24 g 3-methyl-1-phenylpyrazoline was heated with 4.8 g sulfur until hydrogen sulfide ceased to come off. Fractionation of the reaction mass in vacuo then gave 14.2 g (61%) 1-phenyl-3-methylpyrazole.

B. p. 139-140° (19 mm), m. p. 38° (from ligroine) [11, 12].
Found %: N 17.91, 17.97. $C_{10}H_{10}N_2$. Calculated %: N 17.70.

1,3-Diphenylpyrazole. 9.3 g 1,3-diphenylpyrazoline was heated with 1.32 g sulfur until hydrogen sulfide ceased to come off. The reaction mass was then poured into 40 ml methanol. There was obtained 8.1 g (88%) crude pyrazole which after 3 recrystallizations from alcohol had m.p. 85° [13].

Found %: N 12.72, 12.79. $C_{15}H_{12}N_2$. Calculated %: N 12.72.

1,5-Diphenylpyrazole. 13.4 g 1,5-diphenylpyrazoline was heated in a small Claisen flask with 2.52 g sulfur until hydrogen sulfide ceased to come off. The reaction mass was distilled in vacuo to give 11.2 g (84%) 1,5-diphenylpyrazole.

B. p. 182-183° (8 mm), m. p. 56° (from ligroine) [14].
Found %: N 12.59, 12.64. $C_{15}H_{12}N_2$. Calculated %: N 12.72.

1,3,5-Triphenylpyrazole. 20.8 g benzylideneacetophenone and 10.8 g phenylhydrazine were heated in a mixture of 15 ml alcohol and 15 ml benzene. (Two drops of formic acid were also added if an exothermic

reaction did not ensue.) After 1 hour's heating, the solvent was distilled off in the vacuum of a water jet pump until the temperature had reached 200°. To the residue was then added 3.1 g sulfur and the mixture was heated until a gentle stream of hydrogen sulfide was evolved. When gas ceased to come off (after about an hour), the reaction mass was poured into 200 ml methanol and stirred; the methanol was decanted off from the resinous mass. After standing, the methanolic liquor deposited crystals of 1,3,5-triphenylpyrazole (20 g, 67%) with m.p. 140° (from a 1 : 4 mixture of benzene and isooctane) [15].

Found %: N 9.45, 9.48, 9.54. $C_{21}H_{16}N_2$. Calculated %: N 9.45.

1-Phenyl-3-tert-butylpyrazole. 10.1 g 1-phenyl-3-tert-butylpyrazole was heated with 1.8 g sulfur until hydrogen sulfide ceased to come off. The reaction mass was then distilled in vacuo. Two fractional distillations gave 6.1 g of substance with b. p. 151° (18 mm), m. p. 74° (from ligroine) [8].

The picrate had m. p. 116° (from 50% alcohol).

Found %: N 16.77, 16.83. $C_{13}H_{16}N_2 \cdot C_6H_3N_3O_7$. Calculated %: N 16.90.

1-Phenyl-3-acetaminopyrazole. 2.4 g sulfur was gradually stirred into 15.08 g melted 1-phenyl-3-acetaminopyrazoline [8] in a small beaker. Heating was continued until hydrogen sulfide ceased to come off. The mass was then dissolved in 80 ml methanol and boiled 30 minutes with 3 g active carbon. The filtrate was evaporated to give 13.1 g (87%) 1-phenyl-3-acetaminopyrazole, m. p. 128°.

Found %: N 20.91, 20.96. $C_{11}H_{11}ON_3$. Calculated %: N 20.88.

1-Phenyl-3-aminopyrazole. 15.9 g 3-amino-1-phenylpyrazoline [8] was heated with 3.2 g sulfur in a small Claisen flask on an oil bath at 200° for 2 hr. Fractional distillation of the mass gave 6.1 g (39%) of a 167-170° (8 mm) fraction. After numerous recrystallizations from octane, the product had a constant melting point of 90°. The literature reports m. p. 101° (from water) [16].

Found %: N 26.41, 26.63; C 67.46, 67.61; H 5.80, 5.95. $C_9H_9N_3$. Calculated %: N 26.39; C 67.91; H 5.69.

Picrate: m. p. 158-159° (from alcohol).

Found %: N 21.66, 22.03. $C_9H_9N_3 \cdot C_6H_3O_7N_3$. Calculated %: N 21.64.

Acetylation of this amine by boiling with a 3-fold excess of acetic anhydride for 5 hr gave 3-acetamino-1-phenylpyrazole with m. p. 129°. No depression of melting point in mixture with the above-described preparation.

SUMMARY

1. It was shown that N-phenylpyrazolines are dehydrogenated by sulfur to N-phenylpyrazoles.

2. It was established that an acetamino group in the ring does not appreciably complicate the reaction.

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THE SYNTHESIS OF 3-METHYL-1-THIAINDAN AND THE
REARRANGEMENT OF ALLYLARYLSULFONES

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In the investigation of the composition and properties of the sulfur compounds present in petroleums, interest is attached to the synthesis as model substances of the so-called semiaromatic bicyclic compounds, in particular of homologs of 1-thiaindan with substituents in the hydrogenated ring. The present work is concerned with the synthesis of the previously undescribed 3-methyl-1-thiaindan.

Backer and Dost [1] found that heating of allyl phenyl sulfone with sulfuric acid in presence of boron fluoride leads to isomerization with formation of a product to which the structure of 3-methyl-2,3-dihydrothionaphthene sulfone was assigned. Reduction of the sulfone group in this compound might have been expected to lead to the compound of interest to us — 3-methyl-1-thiaindan (3-methyl-2,3-dihydrothionaphthene). However, reduction with lithium aluminum hydride in ether of the "product of cycloisomerization" of allyl phenyl sulfone — which we prepared by the method given by the above authors — did not give expected 3-methyl-1-thiaindan but propyl phenyl sulfone in nearly quantitative yield. It followed that the compound assumed by Backer and Dost to be 3-methyl-1-thiaindan sulfone could not have had a bicyclic structure; we established that the product of isomerization of allyl phenyl sulfone was propenyl phenyl sulfone. The reaction of boron fluoride-containing sulfuric acid on allyl p-tolyl sulfone similarly leads to propenyl p-tolyl sulfone; reduction of the latter with lithium aluminum hydride gives propyl p-tolyl sulfone.

Cyclization to 3-methyl-1-thiaindan sulfones consequently does not occur when boron fluoride-containing sulfuric acid acid acts on allyl aryl sulfones. Under the conditions described, allyl aryl sulfones isomerize to propenyl compounds in similar fashion to the thermal rearrangement of allyl aryl sulfides previously described by us [2].

$$ArSCH_2CH{=}CH_2 \xrightarrow{H_2SO_4,\ BF_3} ArSCH{=}CHCH_3 \xrightarrow{LiAlH_4} ArSCH_2CH_2CH_3;$$

$$Ar = C_6H_5,\ p\text{-}C_6H_4CH_3.$$
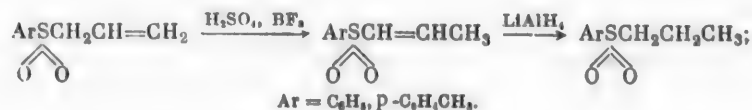
The investigation demonstrated the impossibility of preparing 1-thiaindans by cyclization of allyl aryl sulfides and sulfones. Further work in this field was directed toward the preparation of 1-thiaindans through the thiaindenes (benzothiophenes) and their derivatives. We obtained 3-methyl-1-thiaindan by reduction of 3-methylthiaindene sulfone. The steps in the synthesis and the yields at each step are shown below:
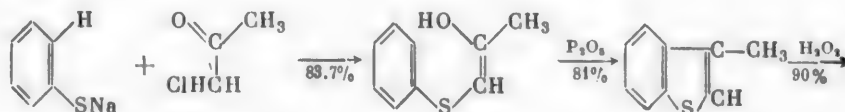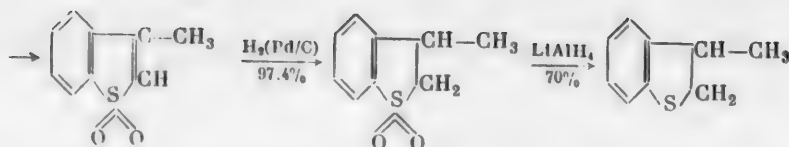
Reduction of thiaindene (thionaphthene) to thiaindan by the action of sodium in alcohol does not go smoothly; the yield of 1-thiaindan is low [3]. It could be assumed that 3-methylthiaindene will be reduced with very much greater difficulty than thiaindene. Reduction of thiaindene sulfone with lithium aluminum hydride gave 1-thiaindan in good yield. As was shown by Bordwell and McKellin [4], the double bond is here at first reduced slowly, and later the sulfone group is reduced very quickly.

On the other hand, the attempt to reduce 3-methylthiaindene sulfone with lithium aluminum hydride revealed that the double bond is not reduced at all; we isolated only 3-methylthiaindene which, like thiaindene [4], does not react with lithium aluminum hydride.

The double bond of 3-methylthiaindene sulfone could be reduced by hydrogen under pressure in presence of palladized carbon under more drastic conditions than those described [5] for thiaindene sulfone. The resulting 3-methyl-1-thiaindan sulfone is easily and rapidly reduced by lithium aluminum hydride to give 3-methyl-1-thiaindan.

The structure of 3-methyl-1-thiaindan (and in turn of the product of cyclization of phenylacetonyl sulfide) was established by hydrodesulfurization over Raney nickel.
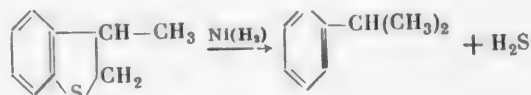
The yield of 3-methyl-1-thiaindan, calculated on the thiophenol, is 41%. The synthesis is therefore of preparative interest.

EXPERIMENTAL

Rearrangement of allyl aryl sulfones to propenyl aryl sulfones. 0.16 mole allyl phenyl sulfone and 3.5 ml 12% solution of BF_3 in conc. H_2SO_4 were heated 3 hr in a sealed tube at 105°. After cooling, the mixture was poured into water, and propenyl phenyl sulfone separated out. Yield of crude product 43%, m. p. 72-73° (from alcohol).

A mixed melting test with propenyl phenyl sulfone prepared by oxidation of propenyl phenyl sulfide by another method [2] did not give a depression.

Found %: C 59.33; H 5.55; S 17.56. $C_9H_{10}O_2S$. Calculated %: C 59.34; H 5.49; S 17.58.

0.028 mole allyl p-tolyl sulfone and 6 ml 12% solution of BF_3 in H_2SO_4 were heated as above. Yield of crude propenyl p-tolyl sulfone 50%. The product was distilled in vacuo and then recrystallized from dilute (3 : 1) alcohol. M. p. 99-100.5°. A mixture with propenyl p-tolyl sulfone prepared by oxidation of propenyl p-tolyl sulfide did not exhibit a depression of melting point.

Found %: C 61.24; H 6.16; S 16.26. $C_{10}H_{12}O_2S$. Calculated %: C 61.22; H 6.12; S 16.32.

To 0.19 mole lithium aluminum hydride in 100 ml absolute ether was gradually added 0.027 mole propenyl phenyl sulfone prepared by isomerization of allyl phenyl sulfone. The mixture was refluxed 1 hr and then treated with water and dilute hydrochloric acid (until the solid dissolved). The ethereal layer was separated, the aqueous layer was extracted with ether, the combined ether extracts were washed with dilute sodium hydroxide solution and then with water, and dried with calcined potassium carbonate. The solvent was driven off to leave a residue of crude propyl phenyl sulfone; yield 93%. Distillation gave propyl phenyl sulfone with b.p. 156-158° at 4 mm, m. p. 43.5-44.5° (from isooctane); yield 78.5%. The literature [6] gives m. p. 45°.

Found %: C 58.99; H 6.56; S 17.39. $C_9H_{12}O_2S$. Calculated %: C 58.70; H 6.52, S 17.39.

0.008 mole propenyl p-tolyl sulfone was similarly reduced with lithium aluminum hydride. Yield of propyl p-tolyl sulfone 75%. M. p. 52.5°. The literature [7] gives m. p. 53°.

Found %: C 60.65; H 7.04; S 16.00. $C_{10}H_{14}O_2S$. Calculated %: C 60.61; H 7.07; S 16.19.

Synthesis of 3-methyl-1-thiaindan. Phenylacetonyl sulfide was prepared, as described by Werner [8], by the action of chloroacetone on aqueous sodium thiophenate. Yield 83.7%, b. p. 142-143° at 17 mm, m. p. 33-34°. Heating of phenylacetonyl sulfide with P_2O_5 [8] gives 3-methylthiaindene. Yield 81%, b. p. 127-129° at 25 mm, $n^{20}D$ 1.6236.

Oxidation of 3-methylthiaindene with hydrogen peroxide, as described by Werner [8], gave 3-methyl-thiaindene sulfone. Yield of crude product 90%, m. p. 143-144°, rising to 145-146° after recrystallization from alcohol.

0.04 moles 3-methylthiaindene sulfone was dissolved in 200 ml of a mixture of equal volumes of ether and benzene. To the solution was added 0.4 mole lithium aluminum hydride in 300 ml ether. The mixture was boiled 38 hr. It was worked up as described for the reduction of propenyl phenyl sulfone; distillation in vacuo gave a fraction with b. p. 124-129° at 25 mm. Yield 64%, calculated on the 3-methyl-1-thiaindene. The ultraviolet absorption spectrum is identical with that of 3-methylthiaindene *. Oxidation of this fraction with hydrogen peroxide gave 3-methylthiaindene sulfone; yield 68%.

0.08 mole 3-methylthiaindene sulfone in 750 ml alcohol was hydrogenated in presence of 8 g Pd on carbon (the catalyst was prepared by the method of [9], modified in that the weight of the palladium was 7% of the weight of the catalyst) at room temperature and an initial hydrogen pressure of 35 atm for 10 hr. The mixture was filtered, and the filtrate was concentrated to about 30 ml and diluted with water. Yield of crude 3-methyl-1-thiaindan sulfone 97%. M.p. 57-58° (from 1.3 alcohol to water).

Found %: C 59.50; H 5.58; S 17.28. $C_9H_{10}O_2S$. Calculated %: C 59.34; H 5.49; S 17.58.

0.22 mole 3-methyl-1-thiaindan sulfone in 200 ml ether was added to a solution of 0.28 mole lithium aluminum hydride in 400 ml ether at such a speed that the ether boiled. The mass was then stirred for 10 minutes. More prolonged heating increased the quantity of secondary products that were free of sulfur. The excess of lithium aluminum hydride was decomposed with water, the mixture was steam-distilled, and the reaction product was extracted from the distillate with ether. The ether extracts were dried with calcined magnesium sulfate; the residue after distillation of the solvent was distilled in a 16-plate column and 3-methyl-1-thiaindan was isolated with b. p. 94.5° at 4.5 mm; $n^{20}D$ 1.5953. Yield 70%.

Found %: C 72.41; H 7.21; S 20.50. $C_9H_{10}S$. Calculated %: S 72.00; H 6.66; S 21.33.

Judging by its elemental composition, the above preparation of 3-methyl-1-thiaindan contains about 4% of hydrocarbon impurity. The product was purified for analysis via the complex with mercuric chloride. 0.066 mole 3-methyl-1-thiaindan was added to a solution of 0.33 mole mercuric chloride in 500 ml alcohol, and the mixture was boiled 0.5 hr. The complex came down when the mixture was cooled with ice and salt and was recrystallized from isooctane. Yield 87%, m. p. 115-116.5°; after recrystallization from alcohol the yield of complex was 57%; m. p. 116-117°.

Found %: C 15.52; H 1.43; $C_9H_{10}S \cdot 2HgCl_2$. Calculated %: C 15.58; H 1.44.

0.045 mole of the 3-methyl-1-thiaindan – mercuric chloride complex, recrystallized from isooctane, was treated with excess of 15% hydrochloric acid, and the mixture was steam-distilled. 3-Methyl-1-thiaindan was extracted from the distillate with ether; the extracts were washed with sodium carbonate, then with water and dried with calcined magnesium sulfate. Distillation from a Claisen flask yielded pure 3-methyl-1-thiandan. Yield 67%.

B. p. 96.5-97° at 6 mm, d^{20}_4 1.0980. $n^{20}D$ 1.5969, MR_D 46.40; calc. 45.94, EMR_D 0.56.
Found %: C 72.09; H 6.75; S 21.11. M 148.7. $C_9H_{10}S$. Calculated %: C 72.00; H 6.66; S 21.33; M 150.

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*The ultraviolet adsorption spectra of 3-methylthiaindene and of the product of reduction of 3-methylthiaindene sulfone were obtained in the optical laboratory of the Institute of Heteroorganic Compounds of the Acad. Sci. USSR.

0.01 mole 3-methyl-1-thiaindan was oxidized in acetic acid with 3.1 g 27.3% hydrogen peroxide for 1 hr at 70°. 3-Methyl-1-thiaindan sulfone with m. p. 57-58° was isolated. A mixture with the sulfone prepared by hydrogenation of 3-methylthiaindene sulfone did not give a depression of melting point. Yield 70%.

0.02 mole 3-methyl-1-thiaindan in 150 ml alcohol was boiled 11 hr with Raney nickel obtained by the method of [10] from 85 g Raney alloy. To the mixture was added 50 ml water, and the alcohol and water were distilled off; 100 ml dilute (1 : 1) alcohol was added to the residue, and distillation was again carried out. The cumene content of the distillate (84% of the theoretical) was determined by spectrophotometry*.

SUMMARY

1. Heating of allyl aryl sulfones with boron fluoride-containing sulfuric acid leads to isomerization to propenyl aryl sulfones.

2. Lithium aluminum hydride reduces only the sulfone group of 3-methylthiaindene sulfone. In this respect the latter behaves differently from thiaindene sulfone.

3. The previously unknown 3-methyl-1-thiaindan was synthesized by stepwise reduction of 3-methylthiaindene sulfone.

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*Analysis by T. S. Novozhilova using the "Uvispek" ultraviolet spectrophotometer.
**Original Russian pagination. See C.B. Translation.

REACTION OF ETHYLENEIMINO-1,4-BENZOQUINONES WITH AMINES

I. THE REACTION BETWEEN ETHYLENEIMINO-1,4-BENZOQUINONES WITH SECONDARY AMINES

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Ethyleneimine and its C-substituted derivatives react with greater difficulty than ethylene oxide with ammonia and amines. Thus, ethyleneimine remains unchanged after boiling with piperidine for over three weeks [1]. Formation of a product of closure of the three-membered ring was not observed when ethyleneimine was heated with excess of diethylamine at 110-120° in a sealed tube for 3.5 hr [2]. Cleavage of ethyleneimine and its C-substituted derivatives with formation of the corresponding ethylenediamines could be effected by heating them in an autoclave under pressure [3, 4] or in presence of catalysts such as aluminum chloride [5, 6], amine hydrochlorides and other amines salts [2], and by heating for many hours in a sealed tube at elevated temperature and pressure in presence of ammonium chloride [7].

Very little has been published about the cleavage of N-substituted ethyleneimines by amines. There have been references to reactions between N-acyl and N-sulfonyl derivatives of ethyleneimine, ethyleneurea and ethyleneurethane on the one hand and amines on the other (these reactions have been described only in German patents [8, 9]) and to the cleavage of 2,5-dichloro-3,6-diethyleneiminoquinone by piperidine [10].

In the present work, we studied the reaction of 2,5-diethyleneimino-1,4-benzoquinones, 2,5-dichloro- and 2,5-diethoxy-3,6-diethyleneimino-1,4-benzoquinones with secondary amines.

The reaction between ethyleneiminoquinones and secondary amines can go in two directions:

$R = H, Cl, OC_2H_5$; $R' =$ amine residue
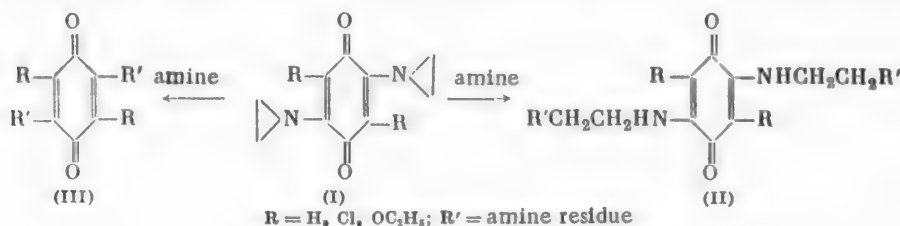
The reaction of ethyleneiminoquinones with secondary amines usually goes smoothly and with satisfactory yields when heating of the diethyleneiminoquinones is carried out for a relatively short period with excess amine (on the average with 5 times the calculated quantity) in a medium of methyl alcohol or in the absence of a solvent. In two cases (reactions of 2,5-diethyleneiminoquinone and 2,5-dichloro-3,6-diethyleneiminoquinone with diethylamine) it was necessary to use the amine hydrochloride as a catalyst.

Our experimental conditions and the products obtained are set forth in Table 1. The physical properties of the products are shown in Table 2.

We see from Table 1 that the reaction between ethyleneiminoquinones and amines goes mainly in the direction of cleavage of the ethyleneimine rings with formation of the corresponding diamines. The rate of this reaction is determined in considerable measure by the nature of the substituent at the ring of the ethylene-iminoquinones. Cleavage of the three-membered rings of 2,5-dichloro-3,6-diethyleneiminoquinone goes with the greatest facility and with the highest yields of reaction products. Cleavage of the ethyleneimine rings of 2,5-diethoxy-3,6-diethyleneiminoquinone calls for more prolonged heating of the reaction mixture, and yields

TABLE 1

Interaction of Ethyleneiminoquinones with Amines

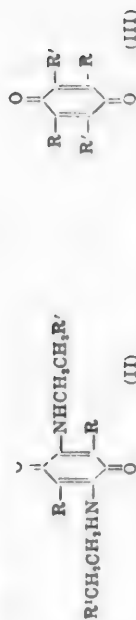| Ethyleneimino-quinone (I)	Amine	Duration of reaction (in minutes)	Solvent	Yield (in %)	
				(II)	(III)
R = H	Piperidine	30	Without solvent	60	—
		10	CH_3OH	—	60
	Morpholine	450	CH_3OH	29	71
		30	CH_3OH	34	66
	Diethylamine	960	Without solvent	—	—
		360	CH_3OH	20	—
		120	CH_3OH	57	—
	Methylaniline	240	CH_3OH	72	—
R = Cl	Piperidine	30	CH_3OH	80	—
		10	Without solvent	60	—
	Morpholine	10	" "	80	—
	Diethylamine	720	" "	—	—
		660	CH_3OH	57	—
	Methylaniline	210	CH_3OH	80	—
		150	CH_3OH	43	—
		90	CH_3OH	—	—
		10	Without solvent	86	—
$R = OC_2H_5$	Piperidine	120	CH_3OH	27	--
		60	Without solvent	55	—
		30	" "	—	-

are lower. Concerning 2,5-diethyleneiminoquinone, its reaction with amines like piperidine and morpholine leads, apart from the usual cleavage reaction, to replacement of the residues of the ethyleneimine rings by residues of piperidine or morpholine with formation of 2,5-dipiperidyl- and 2,5-dimorpholinylquinones. The structure of these compounds was confirmed by the absence of depression of melting point in admixture with compounds synthesized from quinone and piperidine [11] or morpholine [13].

The literature mentions only one case * of displacement of one amino residue by another in the molecule of an aminoquionone, namely the formation of 2,5-dimorpholinylquinone by the action of morpholine on mono-anilinoquinone [13]. These reactions are also interesting in that they enlarge the relatively small and neglected field of reactions in which certain group are displaced by others [10, 15-18], in particular amine residues by other amine residues in substituted quinones.

The facility of cleavage of ethyleneimine rings evidently also depends on the basicity of the reacting amine. Ethyleneimine rings of quinones are most easily cleaved by heterocyclic amines, namely morpholine and piperidine ($K_b^{25°} = 1.6 \times 10^{-3}$); they are cleaved with relative difficulty by the very weakly basic methyl-

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*A very recent publication [14] refers to the displacement of the dimethylamino residue by the ethyleneimino residues in 2,5-di-(dimethylamino)-3,6-dichloroquinone with formation of 2,5-diethyleneimino-3,6-dichloroquinone, and also to the displacement of ethylenimino residues by n-butylamino residues in 2,5-diethylene-iminoquinone with formation of 2,5-di-(butylamino)-quinone.

TABLE 2

Products of Reaction of Ethyleneiminoquinones with Amines

Structures (II) and (III)

Compound prepared	M. p. (solvent)	Color of crystals	Found (in %)			Calc. (in %)		
			C	H	N	C	H	N
II } (R=H, R' = -N⟨⟩)	164—165° (hexane)•	Bright-red	66.55	8.95	—	66.63	8.94	—
III }	177—178 (methanol)•	Reddish-brown	69.98	8.10	9.95	70.04	8.08	10.21
II } (R=H, R' = -N⟨O⟩)	185—189 (methanol)••	Light-red	59.10	7.62	—	59.32	7.74	—
III }	246—247 (methanol)•••	Dark-red	60.10	6.56	10.21	60.40	6.52	10.07
II (R=H, R = -N(C₂H₅)₂)	133—134 (hexane)••••	Light-red	64.03	9.63	—	64.20	9.58	—
II (R=H, R' = -N⟨CH₃ / C₆H₅⟩)	204—205 (methanol-chloroform)	Dark-red	71.02	6.86	13.99	71.25	6.98	13.85
II (R=Cl, R = -N⟨⟩)	187—188 (methanol)•••••	Brown	56.00	6.78	—	55.95	7.04	—
II (R Cl, R' = -N(C₂H₅)₂)	187.5—188 (methanol-chloroform)	Light-brown	49.92	6.01	—	49.88	6.05	—
II (R=Cl, R' = -N⟨CH₃ / C₆H₅⟩)	133—134 (methanol)	Dark-red	53.42	7.30	—	53.33	7.46	—
II (R=Cl, R' = -N⟨O⟩)	177—178 (methanol-chloroform)	Reddish-brown	60.89	5.68	—	60.88	5.54	—
II (R=OC₂H₅, R' = -N⟨⟩)	103—110 (hexane)	Dark-green	64.26	8.99	—	64.01	8.90	—

•Literature data [11]; m. p. 172°.
•Literature data [12]; m. p. 189-190°.
••Literature data [13]; m. p. 248-249°.
•••Literature data [12]; m. p. 134-135°.
••••Literature data [10]; m. p. 188-189°.

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aniline ($K_b^{25°} = 5 \times 10^{-10}$). On the other hand, it is suprising that such a fairly strong base like diethylamine ($K_b^{25°} = 9.6 \times 10^{-4}$) reacts very slowly both with 2,5-diethyleneiminoquinone and with 2,5-dichloro-3,6-diethyleneiminoquinone. In these cases a hydrochloride must be added as catalyst.

Comparison of our results with those in the literature on the cleavage of ethyleneimine and its C-substituted derivatives [1-7] indicates that the latter are more stable than the ethyleneimino rings of ethyleneiminoquinones. The lower stability of the latter may be due to the presence of a quinoid ring at the nitrogen of the ethyleneimine ring.

The enhanced resistance of ethyleneimine and its C-substituted derivatives toward the action of amines is evidently explicable in terms of the "aromatic" character of ethyleneimine (A). In recent years an aromatic character has been attributed [19, 20] to ethyleneimine on the basis of the determination of its thermodynamic constant (by measurement of the pH of its aqueous solutions) and on the basis of spectroscopic investigation of its hydrogen bond.

The presence of an electrophilic grouping at the nitrogen of ethyleneimine (as in the case of ethyleneiminoquinones) must, in our opinion, lead to electron shifts in the ethyleneimine ring and thereby destroy its "aromatic character" (B).

(A)   (B)
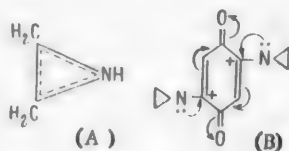
Depending on the substituent in the ring, e.g. chlorine or ethoxy, the electronic shift in the ethyleneimine ring toward the quinone will vary. When chlorine is present in the quinone ring, the shift of electrons from the nitrogen of the ethyleneimine ring to the quinone nucleus will be more intensive (C) than in the case of the unsubstituted quinone, so that the stability of the three-membered ring is weakened and its becomes more susceptible to cleavage by amines. Conversely, the introduction of an ethoxy group into the quinone ring causes the shift of the electrons of the nitrogen of the ethyleneimine ring towards the quinone ring to be weaker [D] than in the case of the unsubstituted quinone; consequently the three-membered ring of this compound will be more resistant to amines.

(C)   (D)
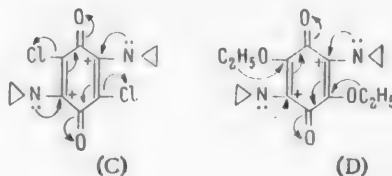
EXPERIMENTAL

Reaction of 2,5-diethyleneiminoquinone (I, R = H) with piperidine. a) A suspension of 0.3 g (I, R = H) in 1.5 ml piperidine was heated to the boil for 30 min. The reddish brown solution was evaporated to dryness in vacuo. The residue was extracted with hexane to give 2,5-dipiperidylethylaminoquinone (II, R = H, R' = NC_5H_{10}).

b) A suspension of 0.2 g (I, R = H) in a mixture of 2 ml piperidine and 2 ml methanol was heated to the boil for 10 min. On cooling, the dark cherry-red solution deposited reddish brown 2,5-dipiperidylquinone (III, R = H, R' = NC_5H_{10}). A mixture of the latter with the 2,5-dipiperidylquinone obtained from the quinone and piperidine did not undergo a depression of melting point.

Reaction of 2,5-diethyleneiminoquinone with morpholine. a) A suspension of 0.2 g (I, R = H) in a mixture of 2 ml morpholine and 2 ml methanol was heated to the boil for 7.5 hr. The color of the solution changed from yellow-orange to brown. The precipitate was filtered. 2,5-dimorpholinylquinone (III, R = H, R' = NC_4H_8O) was obtained.

The melting point of a mixture of this compound with 2,5-dimorpholinylquinone prepared from quinone and morpholine was not depressed. From the mother liquor, after concentration, was isolated 2,5-di-(morpholinyl-ethylamino)-quinone (II, R = H, R' = NC_4H_8O).

b) 0.3 g (I, R = H), 3 ml morpholine and 3 ml methanol were heated to the boil for 30 min. A mixture with the same properties as in experiment (a) was obtained.

Reaction of 2,5-diethyleneiminoquinone with diethylamine. a) A mixture of 0.2 g (I, R = H) and 2 ml diethylamine was heated 16 hr at the boil. The starting substance was recovered unchanged.

b) A mixture of 0.2 g (I, R = H), 1.5 ml diethylamine and 1.5 ml methanol was boiled 6 hr. 2,5-Di-(diethylaminoethylamino)-quinone (II, R = H, R' = NC_4H_{10}) was obtained.

c) A mixture of 0.2 g (I, R = H), 1.5 ml, diethylamine, 1.5 ml methanol and 0.01 g diethylamine hydro-chloride was boiled 2 hr. The same compound as in (b) was obtained.

Reaction of 2,5-diethyleneiminoquinone with methylaniline. A mixture of 0.6 g (I, R = H), 6 ml methyl-aniline and 6 ml methanol was boiled 4 hr. 2,5-Di-(methylanilinoethylamino)-quinone (II, R = H, R' = NC_7H_8) was obtained.

Reaction of 2,5-dichloro-3,6-diethyleneiminoquinone (I, R = Cl) with piperidine. a) A mixture of 0.2 g (I, R = Cl), 1.5 ml piperidine and 1.5 ml methanol was boiled 30 minutes to give 2,5-dichloro-3,6-di-(piperi-dylethylamino)-quinone (II, R = Cl, R' = NC_5H_{10}). A mixture of the product with the starting substance (m.p. 188-189°) melted at 162-165°.

b) A mixture of 0.2 g (I, R = Cl) and 2 ml piperidine was heated at the boil for 10 min. The same sub-stance as in experiment a) was obtained.

Reaction of 2,5-dichloro-3,6-diethyleneiminoquinone with morpholine. A mixture of 0.2 g (I, R = Cl) with 1.5 ml morpholine was boiled 10 min to give 2,5-dichloro-3,6-di-(morpholinylethylamino)-quinone (II, R = Cl, R'=NC_4H_8O). A mixture of the product with the starting substance (m. p. 188-189°) melted at 160-163°.

Reaction of 2,5-dichloro-3,6-diethyleneiminoquinone with diethylamine. a) A suspension of 0.2 g (I, R = Cl) in 1.5 ml diethylamine was boiled 12 hr. The starting substance was recovered unchanged.

b) A mixture of 0.3 g (I, R = Cl), 2.2 ml diethylamine, 2.2 ml methanol and 0.01 g diethylamine hydro-chloride was boiled 11 hr to give 2,5-dichloro-3,6-di-(diethylaminoethylamino)-quinone (II, R = Cl, R' = NC_4H_{10}).

Reaction of 2,5-dichloro-3,6-diethyleneiminoquinone with methylaniline. a) A mixture of 0.2 g (I, R = Cl), 1.7 ml methylaniline and 2 ml methanol was boiled 1.5 hr. The starting substance was recovered un-changed. Heating of the mixture for 2.5 and 3.5 hr gave 2,5-dichloro-3,6-di(methylanilinoethylamino)-quinone (II, R = Cl, R' = NC_7H_8).

b) A mixture of 0.2 g (I, R = Cl) and 3.5 ml methylaniline was heated 10 min at 135°. The same pro-duct as in experiment a) was obtained.

Reaction of 2,5-diethoxy-3,6-diethyleneiminoquinone with piperidine. a) A mixture of 0.3 g (I, R = OC_2H_5), 3 ml piperidine and 3 ml methanol was boiled 2 hr to give 2,5-diethoxy-3,6-di-(piperidylethylamino)-quinone (II, R = OC_2H_5, R' = NC_5O_{10}).

b) A mixture of 0.2 g (I, R = OC_2H_5) and 2 ml piperidine was boiled for 0.5 hr. The starting substance was recovered unchanged. Heating of the mixture for 1 hr led to the same product as in experiment a).

SUMMARY

1. The reaction between 2,5-diethyleneiminoquinone and some of its derivatives and secondary amines was studied. Six new compounds were obtained.

2. It was established that reaction of ethyleneiminoquinones with amines leads both to products of cleavage of the ethyleneimine ring of the type of bis-(alkylaminoethylamino)-quinones and to products of replacement of residues of ethyleneimine by residues of the secondary amines taken into reaction.

3. It was shown that the facility of cleavage of the ethyleneimine ring depends on the character of the substituents in the quinone ring.

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THE POLYCONDENSATION OF SOME N,N'-DIALKYL DERIVATIVES OF 4,4'-DIAMINO-3,3'-DIMETHYLDIPHENYLMETHANE WITH ADIPIC ACID

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In the proeceding communications we described the synthesis and properties of polyamides obtained by polycondensation of 4,4'-diamino-3,3'-dimethyldiphenylmethane and its N,N'-diethyl derivative with adipic acid. *

In the present work we examined reactions of the same type using diamines with larger substituents at the nitrogen (R = C_3H_7, C_4H_9, C_5H_{11}, C_6H_{13} and C_8H_{17}).

We obtained two products on carrying out the polycondensation of propyl- and butyl-substituted diamines with adipic acid: poly-N,N'-dipropyl-3,3'-di-methyldiphenylmethaneadipamide and poly-N,N'-dibutyl-3,3'-dimethyldiphenylmethaneadipamide. Both of the synthesized polyamides are vitreous, faint-yellow products, readily soluble in alcohol, benzene, acetone, formic acid, acetic acid, and tricresol. The specific viscosity of their 0.5% solutions in methanol is 0.05. Poly-N,N'-dipropyl-3,3'-dimethyldiphenylmethaneadipamide melts at 57°; poly-N,N'-dibutyl-3,3'-dimethyldiphenylmethane-adipamide melts at 55°.

We determined the magnitudes of the constant K_m by the light-scattering method: the value for the first polyamide was 10.2×10^{-4}, and for the second 11.1×10^{-4}.

The molecular weights of the two polyamides were between 4500 and 5200. These low values are obviously associated with considerable steric hindrance during polycondensation due to the large sizes of the alkyl substituents at the nitrogen.

The greater solubility and lower melting point of these polymers in comparison with poly-N,N'-diethyl-3,3'-dimethyldiphenylmethaneadipamide may be said to be a consequence of the less rigid packing of the polymer chains.

The change of character of the polycondensation reaction with passage of time was studied by the method of successive sampling, and it was found desirable to carry out the reactions for 5 hr in a nitrogen stream and then for 2 hr in vacuo (3-5 mm). The two hour heating of the reaction mass in vacuo leads to an increase of about 2000 in the molecular weight; further polycondensation in vacuo does not result in any appreciable increase in molecular weight.

Optimum temperature conditions were established in one set of experiments. Condensation of N,N'-dipropyl-4,4'-diamino-3,3'-dimethyldiphenylmethane with adipic acid at 160° leads mainly to a monomeric amide; similarly, reaction of N,N'-dibutyl-4,4'-diamino-3,3'-dimethyldiphenylmethane with adipic acid at 160-180° leads to monomeric amide and only a small quantity of dimer. The optimum temperature for both of the reactions is 260°. At this temperature polyamides with maximum degree of polycondensation (10-12) are obtained with minimum amine and acid numbers.

*See J. Gen. Chem. 27, 775 (1957). [Original Russian pagination. See C.B. Translation.]

As starting components we also used N,N'-diisoamyl-N,N'-dihexyl- and N,N'-dioctyl-substituted diamines. These compounds, which are viscous, faint-yellow liquids, were condensed with adipic acid at 200 and 250°. Completion of the process is favored by higher temperatures (see Table 1). Condensation of N,N'-diisoamyl- and N,N'-dihexyl- derivatives of the diamines with adipic acid at 200° leads to dimers; rise of temperature to

TABLE 1

Polycondensation of Some N,N'-Dialkyl Derivatives of 4,4'-Diamino-3,3'-dimethyldiphenylmethane with Adipic Acid

Starting diamine	Quantity of starting substance (in g)		Reaction temperature	Acid number		Degree of completion	Degree of polycondensation
	diamide	adipic acid		before reaction	after reaction		
N,N'-Diisoamyl-4,4'-di-amino-3,3'-dimethyldi-phenylmethane	3.67	1.46	200°	214	98	0.54	2
	3.67	1.46	250	214	65	0.70	3
N,N'-Dihexyl-4,4'-diamino-3,3'-dimethyldiphenyl-methane	3.95	1.46	200	204	85	0.53	2
	3.95	1.46	250	204	30	0.85	7
N,N'-Dioctyl-4,4'-diamino-3,3'-dimethyldiphenyl-methane	4.52	1.46	200	185	162	0.12	0
	4.52	1.46	250	185	150	0.19	0

250° enables preparation of products with a higher degree of polycondensation: trimers in the case of diiso-amyl-substituted diamine and heptamers when using the dihexyl derivative of 4,4'-diamino-3,3'-dimethyldi-phenylmethane.

Condensation of N,N'-dioctyl-4,4'-diamino-3,3'-dimethyldiphenylmethane with adipic acid (see Table 1) goes mainly to the stage of formation of the monomeric amide.
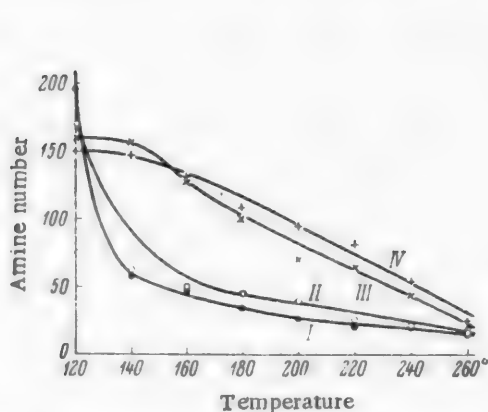

Fig. 1. Relative reactivity of diamines in the polycondensation reaction with adipic acid. For key see footnote for Table 2.
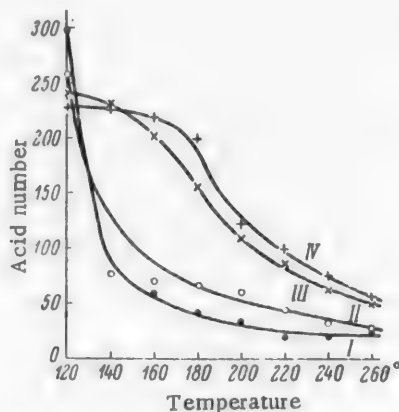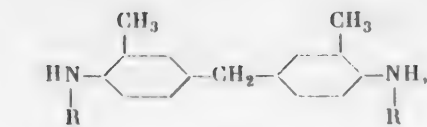

Fig. 2. Relative reactivity of diamines in the polycondensation reaction with adipic acid (as followed by change in acid numbers). For key see footnote on page 667.

On the basis of the data presented in this paper and the preceding papers, we can make some generalizations concerning the synthesis and properties of poly-N,N'-dialkyl-3,3'-dimethyldiphenylmethaneadipamides obtained by condensation of adipic acid with diamines of the general formula:

$$\text{HN} - \overset{\displaystyle \text{CH}_3}{\underset{\displaystyle R}{\bigcirc}} - \text{CH}_2 - \overset{\displaystyle \text{CH}_3}{\underset{\displaystyle R}{\bigcirc}} - \text{NH},$$

where $R = C_2H_5, C_3H_7, C_5H_{11}, C_6H_{13}$ or C_8H_{17}.

These diamines have extremely diverse reactivities since with increasing size of substituent at the nitrogen atom the steric hindrances to reaction increase considerably. When R is C_4H_9 the minimum temperature at which condensation occurs rises from 120 to 160°; the optimum reaction temperature rises from 220-240° to 260-280° (see Figs. 1-3 *); the greater the size of R, the lower the degree of completion of the reaction and the degree
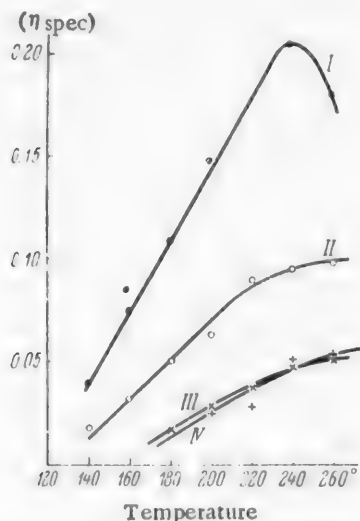

Fig. 3. Specific viscosity of solutions of polyamides (η_{spec}) as a function of the reaction temperature. I) In tricresol solution (0.5%); II, III and IV in methanol solution (0.5%). For key see footnote.
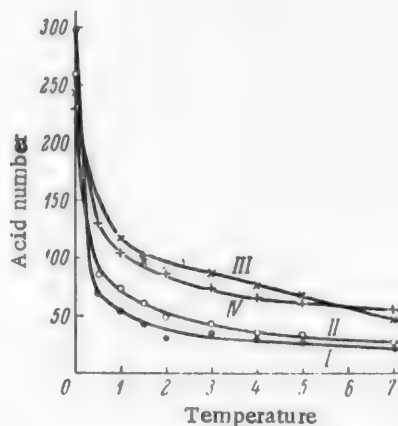

Fig. 4. Acid numbers in dependence on the reaction duration at 260°. For key see footnote.

TABLE 2

Melting Points of Poly-N,N'-dialkyl-3,3'-dimethyldiphenylmethaneadipamides

Polyamide	Melting point
Poly-3,3'-dimethyldiphenylmethaneadipamide	325°
Poly-N,N'-diethyl-3,3'-dimethyldiphenylmethaneadipamide	78
Poly-N,N'-dipropyl-3,3'-dimethyldiphenylmethaneadipamide	57
Poly-N,N'-dibutyl-3,3'-dimethyldiphenylmethaneadipamide	55
Poly-N,N'-dihexyl-3,3'-dimethyldiphenylmethaneadipamide	45

*In Figs. 1-6 curve I corresponds to poly-3,3'-dimethyldiphenylmethaneadipamide, curve II to poly-N,N'-diethyl-3,3'-dimethyldiphenylmethaneadipamide; curve III to poly-N,N'-dipropyl-3,3'-dimethyldiphenyl-methaneadipamide; curve IV to nonyl-N,N'-dibutyl-3,3'-dimethyldiphenylmethaneadipamide.

of polycondensation at any given instant from the start of the process. The progress of the reaction can be followed from the change of the amine and acid numbers and of the specific viscosities of solutions of polyamides (Figs. 4-6). Finally, in the case of N,N'-dioctyl-3,3'-dimethyldiphenylmethane (as we noted above) condensation with adipic acid only goes as far as formation of the monomeric amide.
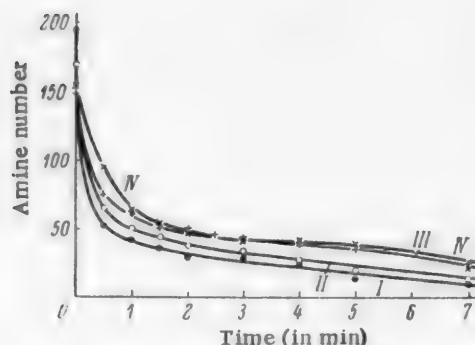

Fig. 5. Amine numbers in dependence on the reaction duration at 260°. For key see footnote for Table 2.
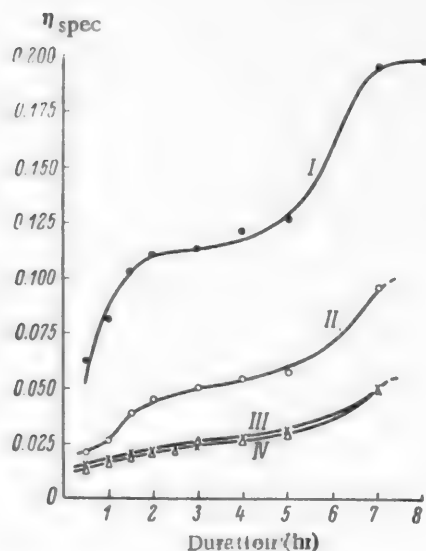

Fig. 6. Specific viscosity of solutions of polyamides (η_{spec}) as a function of the duration of the reaction at 260°. For key see footnote on page 667.

In addition to markedly influencing the polycondensation reaction, the character of the diamines determines in large measure the properties of the polyamides: their solubility, melting point, outward appearance and other properties are bound up with the magnitude of the intramolecular forces and the packing density of the polymeric chains. For example, macromolecules of poly-3,3'-dimethyldiphenylmethaneadipamide are firmly linked by hydrogen bonds. Due to this the polymer is insoluble in common organic solvents and only dissolves in strongly polar solvents (cresol, sulfuric acid). The hydrogen bonds also account for the high melting point of the same polyamide (325°). Finally, the opacity and porcelain-like appearance of poly-3,3'-dimethyldiphenylmethaneadipamide are features associated exclusively with highly ordered structures.

If, however, one of the starting components is an N,N'-alkylated diamine, there is no possibility of formation of hydrogen bonds between the macromolecules. The larger is the substituent at the nitrogen, the more loosely packed are the polymeric chains, and consequently the better the solubility and the lower the melting point (Table 2).

All of the polyamides prepared with N,N'-alkylated diamines are glassy and readily soluble in common organic solvents like benzene, acetone, methanol and ethanol.

EXPERIMENTAL

Polycondensation was effected by charging the mixture of equimolar quantities of diamine and adipic acid into a three-neck flask which was then heated by means of Wood's alloy. The reaction was conducted at 250° for 7 hr (5 hr in a stream of carbon dioxide and 2 hr in vacuo).

A large number of experiments were run with the objective of establishing the optimum reaction time and temperatures. These experiments were performed in small test tubes with side tubes. The reaction course was followed by withdrawal of successive samples and determination of the acid and amine numbers of the products, as well as of the specific viscosities of their 0.5% alcoholic solutions.

Results of the experiments for the purpose of ascertaining the optimum polycondensation conditions are presented in Figs. 1 to 6.

SUMMARY

1. Poly-N,N'-dipropyl-, poly-N,N'-dibutyl-, poly-N,N'-diisoamyl- and poly-N,N'-dihexyl-3,3'-dimethyldiphenylmethaneadipamide were synthesized and characterized for the first time.

2. Optimum conditions were found for the polycondensation of N,N'-dipropyl-4,4'-diamino-3,3'-dimethyldiphenylmethane and N,N'-dibutyl-4,4'-diamino-3,3'-dimethyldiphenylmethane with adipic acid.

3. The relative reactivity of 4,4'-diamino-3,3'-dimethyldiphenylmethane and its N,N'-dialkyl derivatives in polycondensation with adipic acid was determined. The properties of the polycondensation products depend on the size of the substituting radical at the nitrogen atom and on the degree of hydrogen bonding.

THE ALKALOIDS OF TRICHODESMA INCANUM

THE STRUCTURE OF INCANINE AND TRICHODESMINE

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G. P. Menschikov and M. Rubinstein [1] isolated 0.1% of the total alkaloids from the above-ground portion of Trichodesma incanum (Bge) DC of the Borraginaceae family; they also separated a pure alkaloid — trichodesmine (0.075%). Alkaline hydrolysis of the latter gave an amino alcohol — retronecine [2] — and products of cleavage of trichodesmic acid. The structure of the latter was established [3].

The seeds and above-ground portion of Trichodesma incanum that we investigated were collected by E. E. Korotkova during the vegatative periods in various districts of Uzbekistan [4]. Different mixtures of bases (in dependence on the degree of ripeness) were obtained from the seeds by continuous extraction with ether and chloroform [5].

The mixture of alkaloids was fractionated by taking advantage of their differing solubility in ether, benzene and acetone. In this way four crystalline bases were isolated. The first was a new substance which we named "incanine" (I). The second is the N-oxide form of incanine; the third was identified as trichodesmine (II), and the fourth as the N-oxide form of trichodesmine.

The quantitative and qualitative composition of the alkaloids in the seeds varies considerably in dependence on the degree of ripeness of the latter and on the place of growth; the composition of the products from the above-ground part of the plants depends on the stage of development (see table).

The tabulated results are in accord with the regularities established by S. Yu. Yunusov: plants of the same variety may contain (depending on the ecological and other factors) different alkaloids. The maximum quantity of the mixture of alkaloids accumulates in the seeds toward the end of vegatation [6].

The alkaloid incanine (I) forms a series of nicely crystallizing salts: hydrochloride, nitrate, platinochloride and picrate. Incanine has the formula $C_{18}H_{27}O_5N$; it contains one double bond and a hydroxyl group; methoxy and methylimino groups were not detected.

Alkaline hydrolysis of the alkaloid gives different results with different hydroxides — potassium or sodium. The reaction yielded acids not mentioned in the literature — incanic and isoincanic acids — as well as an amino alcohol which was identified as retronecine [2].

Incanic and isoincanic acids have the composition $C_{10}H_{16}O_4$; they possess opposite specific rotations. The melting point of a mixture of the acids is depressed. Geometrical isomerism is indicated by the transition of incanic to isoincanic acid and conversely (depending on whether potassium or sodium hydroxide is used). Both of the acids are monobasic saturated compounds containing a lactone grouping as well as a CH_3-C-CH_3 group and two $C-CH_3$ groups. Since we failed to obtain a hydroxydicarboxylic acid from the investigated acids (but only its sodium salt), incanic and isoincanic acids must contain a five-membered lactone ring.

On reduction of the methyl ethers of the investigated acids with $LiAlH_4$, the products were isomeric neutral compounds with three hydroxyl groups and the composition $C_{10}H_{22}O_3$ (III). Oxidation of 1 mole of compound (III) consumes about 1 mole of periodic acid. Formaldehyde was isolated from the reaction products. These

results indicate the presence of a glycolic structure in compound (III); they also indicate that one of the hydroxyl groups formed during reduction of the ester group is primary. The third hydroxyl group, formed in reduction of the lactone grouping, must be primary and must be located at the fourth carbon atom. In incanic and isoincanic acids the hydroxyl group entering into the composition of the lactone is in the α-position to the carboxyl, while the second carboxyl group and the hydroxyl group that form the lactone are γ to one another.

Alkaloid Contents in Various Phases of Growth and in Different Parts of Trichodesma Incanum

Stage of development of plant, locality and time of gathering	Content of total alkaloids (in % of weight of raw material)	Content of individual alkaloids (in % of total alkaloids)		
		incanine	incanine N-oxide	6-trichodesmine and its N-oxide
Start of vegetation	2.04	—	—	69.76
Start of budding	1.29	24.8	—	69.76
Budding and start of flowering	0.43	—	—	60.00
Flowering and start of formation of ovaries	0.5	—	—	30.00
Plant examined by G.P. Men'shikov [1]	0.1	—	—	70.00
Roots in stage of fruiting	0.65	—	—	69.08
Ripe seeds, Kashka-Dar'in region, 1951	2.7	60.0	26.0	1.00
Not fully ripened seeds, Kashka-Dar'in region, [1951]	1.5	47.0	—	—
Ripe seeds, Samarkand region, 1953	2.9	17.0	5.0	66.30
Ripe seeds, Samarkand region, 1954	3.07	17.0	5.0	66.30

The product of oxidation remaining after elimination of formaldehyde gives a positive iodoform reaction. This points to α-orientation of the methyl and carboxyl groups in incanic and isoincanic acids. Most probably both of the methyl groups in the acids are at adjacent carbon atoms.

On the basis of the foregoing facts we assign to the dibasic acid the structure of 2-hydroxy-3,5-dimethyl-hexane-2,4-dicarboxylic acid (IV). Incanic and isoincanic acids (V) are the γ-lactone of this compound.

(V)
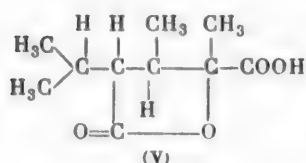
Incanic and isoincanic acids are geometrical isomers because of the different positions of the substituents at the α-carbon atom in relation to the plane of the five-membered lactone ring [7].

With the objective of learning more about the structure of incanine (I), we subjected the product of its acetylation to catalytic hydrogenation. By this means not only was the double bond saturated but the ester group was converted to carboxy with formation of hydroacetoincanine, $C_{20}H_{33}O_6N$, with the properties of an amino acid.

On hydrolysis, hydroacetoincanine is split to the amino alcohol retronecine and incanic and acetic acids.

These results show that incanine, which has the formula $C_{16}H_{25}N(COO)_2(OH)$, is the cyclic diester of retronecine and 2-hydroxy-3,5-dimethylhexane-2,4-dicarboxylic acid.

The results of catalytic reduction of incanine indicate that the lactone-forming carboxyl group is esterified with the secondary alcoholic group of retronecine. Reduction of incanine is accompanied by intramolecular rearrangement with formation of the γ-lactonic acid and amino alcohol [7].

Acid hydrolysis of trichodesmine (II) [8] does not confirm the structure of trichodesmic acid proposed by G. P. Menshikov [3]. We subjected the thioester of trichodesmine to reduction followed by acid hydrolysis, and so obtained retronecanol and trichodesmic acid. These data show that the two hydroxyl groups are arranged side by side or across one carbon atom in the acid portion of the molecule.

Trichodesmic acid $C_{10}H_{16}O_5$ is a monobasic hydroxy acid. Taking the saturation of its molecule into consideration, we can conclude that this acid must be a γ-lactone. G. P. Menshikov and M. M. Rubinshtein [1, 3] established that alkaline hydrolysis of trichodesmine causes breakdown of the latter to lactic acid, carbon dioxide and methyl isobutyl ketone. The latter is the result of ketonic cleavage of α-isopropylacetoacetic or isovalerylacetic acid.

The formation of more than two equivalents of acetic acid and acetone in the oxidation of trichodesmic acid confirms the formation of methyl isobutyl ketone by ketonic cleavage of α-isopropylacetoacetic acid. The latter reacts with lactic acid to form a molecule which is unstable in an alkaline medium and which must have the structure of 2,3-dihydroxy-3,5-dimethylhexane-2,4-dicarboxylic acid (VI). Trichodesmic acid (VII) is accordingly the α-hydroxylactonic acid corresponding to acid (VI) [8].

(VII)
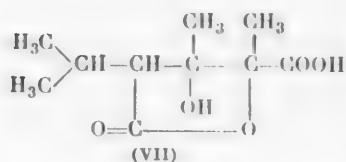
For trichodesmine (II) we gave [8] the structure of the cyclic diester of retronecine and 2,3-dihydroxy-3,5-dimethylhexane-2,4-dicarboxylic acid. In trichodesmine the α-lactone-forming carboxyl group esterifies the secondary alcoholic group of retronecine. During reduction of trichodesmine, when a free carboxyl group appears, intramolecular rearrangement takes place with formation of a γ-lactonic acid and an amino alcohol, similarly to the effect of intramolecular rearrangement during catalytic reduction of incanine (I).

Consequently the structure of trichodesmine (II) differs from that of incanine (I) by one hydroxyl group which is located in the acid part of the molecule. This leads to instability of the acid in an alkaline medium.

(I) R = H; R′ = OH.
(II) R = R′ = OH.

(III) R = CH₂OH; R′ = H.
(IV) R = COOH; R′ = H.
(VI) R = COOH; R′ = OH.
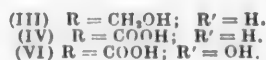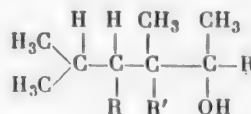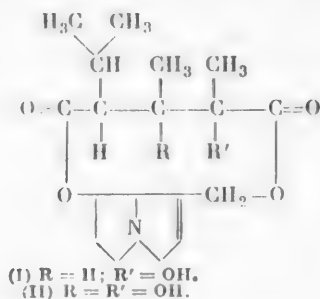
After this work had been completed [5, 7-9], a paper appeared [10] on the isolation of trichodesmine from Crotalaria incei, a plant of the Leguminosae family. The authors of the paper assign the same structure (II) to trichodesmine but with transorientation of the hydroxy groups.

EXPERIMENTAL

Isolation of the alkaloids. 8 kg ripe, pulverized seeds, collected from the Kashka-Dar'in region, were moistened with 8% ammonia solution prior to continuous extraction with ether, followed by exhaustive extraction with chloroform. The ether and chlorofrom extracts were separately worked up with 10% sulfuric acid. The mixture of sulfates of alkaloids from the ether extraction was made alkaline with 25% ammonia and again treated with ether. The mixture of sulfates of bases obtained by chloroform extraction was made alkaline and also treated with ether and then with chloroform. The ether extracts of the alkaloids were combined, and the solvent was driven off, leaving a residue of 137 g of the noncrystalline total bases. The chloroform was removed, leaving 80 g of rapidly crystallizing total bases. The total yield of the mixture of alkaloids was 217 g (2.72%).

The noncrystalline total bases (137 g) crystallized on trituration in benzene. The crystals were quickly collected and washed with benzene. Yield 120 g of technical incanine with m. p. 94-96°. Bases were extracted from the benzene mother liquor with 5% sulfuric acid; the extract was made alkaline and the alkaloids were extracted with ether. Crystals were washed out with acetone from the semicrystalline residue after the ether had been driven off. 2 g trichodesmine was obtained.

The crystalline portion of the bases (80 g) was washed with acetone to give 56 g incanine N-oxide with m.p. 166-168° (decomp.).

From 600 g of unripened seeds from the same locality of growth was obtained 9 g (1.5%) of total alkaloids. Fractionation of the latter gave 4.2 g incanine.

From 600 g ripe seeds originating from the Samarkand region (1953 harvest) was isolated 1 g of trichodesmine N-oxide with m. p. 169-170° (decomp.), 10.5 g trichodesmine, 3 g incanine and 0.8 g incanine N-oxide; the total alkaloids amounted to 17.5 g (2.9%). The same seeds from the 1954 harvest yield 3.07% of total alkaloids.

From 210 g above-ground portions at the initial vegetative stage was extracted 4.3 g (2.04%) of total alkaloids. Fractionation of the latter gave 3 g trichodesmine.

From 20 kg above-ground portions in the budding stage was isolated 258 g (1.29%) of a mixture of bases. 180 g trichodesmine and 64 g incanine were isolated.

From 2 kg above-ground portions at the stage of start of formation of the ovaries was isolated 10 g (0.5%) total alkaloids, fractionation of which gave 3 g trichodesmine.

From 100 g of roots at the fruit-bearing stage was isolated 0.65 g (0.65%) of a mixture of bases. Fractionation of the latter gave 0.45 g trichodesmine.

Incanine was purified by recyrstallization from benzene (1 : 3) or acetone (1 : 1), and via salts. M. p. 97° (from benzene; crystallizes with one molecule of solvent). Easily soluble in alcohol, ether and chloroform, difficultly soluble in water $[\alpha]_D$ −38.76° (c 1.625, alcohol).

Found %: C 64.21; H 8.24; N 4.31; OH 6.4. $C_{18}H_{27}O_5N$. Calculated %: C 64.05; H 8.06; N 4.15; OH 5.04.

Incanine picrate. M. p. 246° (decomp.) (from alcohol).

Found %: C 50.89; H 5.56; N 10.16. $C_{18}H_{27}O_5N \cdot C_6H_3O_7N_3$. Calculated %: C 50.88; H 5.30; N 9.89.

Incanine nitrate. M. P. 182° (from absolute alcohol).

Found %: C 54.08; H 7.22; N 7.16. $C_{18}H_{27}O_5N \cdot NHO_3$. Calculated %: C 54.00; H 7.00; N 7.00.

Incanine hydrochloride. M. p. 199° (from a mixture of alcohol and ether). $[\alpha]_D$ −37.8° (c 2.798, alcohol).

Found %: Cl 9.51. $C_{18}H_{27}O_5N \cdot HCl$. Calculated %: Cl 9.5.

Incanine platinochloride has m. p. 154°.

Incanine methiodide is formed on heating 1 g base in 7 ml methanol with 1.2 ml methyl iodide for 30 min. Yield 0.8 g. M. p. 228° (from ethanol).

Incanine N-oxide is purified by reprecipitation from alcoholic solution with acetone. M. p. 169° (decomp.). The base is soluble in water, alcohol, benzene and chloroform, very poorly soluble in acetone and pyridine.

Found %: C 61.34; H 7.67; N 3.97. $C_{18}H_{27}O_6N$. Calculated %: C 61.16; H 7.70; N 3.97.

Reduction of incanine N-oxide was effected with zinc in hydrochloric acid. Incanine was formed, and the latter was oxidized to the N-oxide with 3% hydrogen peroxide.

Trichodesmine has m. p. 160°.

Trichodesmine picrate. M. p. 228° (from alcohol).

Trichodesmine hydrochloride. M. p. 205° (from alcohol).

Trichodesmine methiodide was prepared by heating the base with methyl iodide in methyl alcohol. M.p. 199-299° (from anhydrous alcohol).

Trichodesmine N-oxide was purified by reprecipitation from alcoholic solution with acetone. M. p. 169-170° (decomp.). Readily soluble in alcohol and water, almost insoluble in acetone and chloroform.

Found %: C 58.57; H 7.31; N 3.65. $C_{18}H_{27}O_7N$. Calculated %: C 58.55; H 7.31; N 3.79.

Reduction of trichodesmine N-oxide with zinc in hydrochloric acid gave trichodesmine. Oxidation of the latter with 3% hydrogen peroxide gave the N-oxide.

Hydrolysis of incanine with potassium hydroxide. 4.5 g of the alkaloid was dissolved in 50 ml 10% methanol solution of potassium hydroxide, and the solution was heated 3 hr on a water bath. The alcohol was driven off, the residue was dissolved in water, acidified and treated with ether. The ether was taken off; the residue (2.5 g) was incanic acid. From the aqueous mother liquor, after it had been made alkaline, an amino alcohol with m. p. 120° was separated which was identified as retronecine.

Incanic acid crystallizes from benzene, benzene-chloroform mixture, and benzene-ligroine mixture. M. p. 163. $[\alpha]_D$ + 25° (c 5.379, ethanol).

Found %: C 59.96; H 8.08; OH 8.6. Equiv. 199.1, 109.5 (back titration). $C_{10}H_{16}O_4$. Calculated %: C 59.95; H 8.05; OH 8.5. Equiv. 200.12, 100.06.

Methyl incanate was obtained by mixing an ethereal solution of 1 g acid with an ethereal solution of diazomethane prepared from 1.2 g nitrosomethylurea. Yield 0.8 g. B. p. 140° at 1 mm. $[\alpha]_D$ + 10.6° (c 1.792, methanol).

Hydrolysis of incanine with sodium hydroxide. 12.5 g incanine and 7 g NaOH were heated 2 hr in 70 ml methyl alcohol. The sodium salt of the acid (3.6 g) came down and was collected. The residue after removal of the methyl alcohol from the liquid portion was dissolved in water, acidified, and treated with ether. There was obtained 3.6 g incanic acid with m. p. 163°. Retronecine (5 g) was isolated from the alkaline mother liquor.

Sodium isoincanate does not melt at 265°. $[\alpha]_D$ −29.5° (c 2.000, water).

3.6 g of the sodium salt was dissolved in a little water and the cooled solution was acidified and then treated with ether. Removal of the ether left 2.8 g isoincanic acid. M. p. 122-123.5° (from water). A mixture of the two acids melted at 105-107°

Isoincanic acid is easily soluble in alcohol, chloroform and water. $[\alpha]_D$ −25° (c 2.375, anhydrous ethanol).

Found %: C 59.83; H 7.79; OH 9.1. Equiv. 200.9, 100.51 (back titration). $C_{10}H_{16}O_4$. Calculated %: C 59.95; H 8.05; OH 9.5. Equiv. 200.12, 100.06.

Methyl isoincanate. To an etheral solution of 0.5 g isoincanic acid was added a solution of diazomethane prepared from 0.6 g nitrosomethylurea. After 2 days the ether was distilled off; the residue crystallized completely (0.45 g). M. p. 44-45° (from dilute methanol). The ester is also formed when hydrogen chloride is passed through a solution of the acid in methyl alcohol. $[\alpha]_D$ − 31.8° (c 2.486, methanol).

Found %: C 61.34; H 8.29. $C_{11}H_{18}O_4$. Calculated %: C 61.68; H 8.41.

Transformation of isoincanic acid into incanic acid. Saponification of methyl isoincanate with 10% methanolic solution of KOH gave incanic acid. In another experiment 0.4 g (1 equiv) of isoincanic acid was heated with a solution of 0.34 g (3 equiv) KOH in 4 ml water. The incanic acid (0.3 g) was extracted with ether.

Transformation of incanic acid into isoincanic acid. 3 g (1 equiv) incanic acid was mixed with a solution of 1.8 g (3 equiv) NaOH in 20 ml methanol. After 1 hr heating, the precipitate (1.2 g) was separated and dissolved in 6 ml water. The aqueous solution was acidified and treated with ether. There was obtained 0.6 g isoincanic acid.

Oxidation of incanic acid (5 g) was performed in a solution prepared from 26 g chromic anhydride and 35 g conc. H_2SO_4 in 500 ml water. After 8 hour ' heating the reaction mixture was steam distilled. 100 g distillate was obtained. The latter was acidified and again steam distilled to give 30 ml of liquid. Treatment of the latter distillate which benzaldehyde gave benzylidene acetone. The combined residues from the steam distillation were acidified; steam distillation was then again carried out and gave another 1400 ml

distillate. Titration of 10 ml of the latter required 3.5 ml 0.1 N KOH, corresponding to 2.3 moles acetic acid per mole of incanic acid. The whole of the distillate was then made alkaline with NaOH and evaporated to dryness. 0.5 g of the dry residue was heated with 0.6 g aniline hydrochloride in an ampoule at 170-175°. After 3 hr the content of the ampoule was dissolved in hot water. Acetanilide with m. p. 112-113° was deposited from the solution on cooling.

Reduction of methyl isoincanate with lithium aluminum hydride. A solution of 6 g methyl isoincanate in 100 ml absolute ether was added dropwise to 2.6 g LiAlH$_4$ in 50 ml ether with continuous stirring in a nitrogen stream. After it had stood 12 hr, the reaction mixture was decomposed at first with water and then with 10% sulfuric acid. The ether layer was washed with water. The aqueous solutions were combined and neutralized; the precipitate was filtered off. The filtrate and the wash liquors were treated with ether. Yield 4.5 g. M. p. 66° (from benzene). [α]$_D$ -10.8° (c 1.017, methanol).

Found %: C 63.18; H 11.49; OH 25.67. C$_{10}$H$_{22}$O$_3$. Calculated %: C 63.12; H 11.65; 3 OH 26.8.

Reduction of methyl incanate with lithium aluminum hydride. Reaction of 3.9 g acid with 3.5 g LiAlH$_4$ gave 3.3 g noncrystalline trihydroxy compound. [α]$_D$ -6.6° (c 1.800, methanol).

Found %: C 63.55; H 11.65. OH 26.02. C$_{10}$H$_{22}$O$_3$. Calculated %: C 63.12; H 11.65; 3 OH 26.8.

Oxidation of the trihydroxy compound with periodic acid. Oxidation of 0.095 g trihydroxy compound of isoincanic acid required 0.890 g HIO$_4$. Oxidation of 0.3858 g trihydroxy compound of incanic acid required 0.3691 g HIO$_4$. The amount of periodic acid before and after the reaction was determined with the aid of arsenic trioxide.

Oxidation of trihydroxy compound with sodium periodate. 1.1038 g trihydroxy compound of isoincanic acid in 40 ml water and 15 ml H$_2$SO$_4$ were shaken 30 min, and the mixture was stood at room temperature 12 hr. The reaction mixture was then transferred to a Wurtz flask fitted with a capillary tube extending to the bottom. The side tube of the flask was joined to a wash bottle filled with a saturated aqueous solution of dimedon. A slow stream of air was passed through the apparatus. Formaldehyde aldimedon deposited in the wash bottle after 2 hr. After elimination of formaldehyde, the aqueous solution was treated with ether and the ether was distilled off. The residue gave a positive iodoform reaction.

Hydroacetonincanine. 3 g incanine (I) in benzene solution was heated 2 hr with acetic anhydride (30 ml) and acetyl chloride (10 ml). After removal of the solvent and excess of reagent, the residue was dissolved in water and extracted from the alkaline solution with ether. The base obtained (2.5 g) was subjected to Adams reduction in an alcoholic medium. Removal of the alcohol left a residue of 2.3 g hydroacetoincanine with m. p. 194-195° (from acetone). Soluble in dilute solutions of ammonia, in sulfuric acid and in water.

Found %: C 62.32; H 8.81; N 3.65. C$_{20}$H$_{33}$O$_6$N. Calculated %: C 62.29; H 8.69; N 3.89.

Hydrolysis of 1.8 g hydroacetoincanine with 10% KOH gave incanic acid (0.9 g), retronecanol (0.5 g) and acetic acid (0.82 mole).

Reduction of incanine. 3 g alkaloid in 50 ml ethanol was shaken with platinum catalyst under pressure in a hydrogen atomosphere. 400 ml hydrogen was taken up in 3 hr. After separation of the catalyst, the alcoholic solution deposited 1.5 g of product with m. p. 156° (from alcohol). Incanic acid was isolated from a sulfuric acid solution of this compound. Retronecanol was obtained from a solution in alkali.

Acid hydrolysis of trichodesmine. 3 g trichodesmine was boiled 16 hr in 50 ml 15% HCl. The solution was cooled and worked up with ether; the residue was 0.9 g trichodesmic acid with m. p. 209° (from ethanol and water).

Found %: C 55.48; H 7.55; OH 15.2. C$_{10}$H$_{16}$O$_5$. Calculated %: C 55.53; H 7.45; 2 OH 15.73. No double bonds present.

From the alkaline mother liquor was recovered 1.5 g of the original base. The alkaline aqueous solution was acidified and evaporated. Retronecine hydrochloride (0.6 g) was extracted from the residue with anhydrous alcohol.

Reaction of trichodesmine with thionyl chloride. Thionyl chloride (15 ml) was added dropwise to 5 g trichodesmine with cooling. After the thionyl chloride had been distilled off, the residue (6 g) crystallized.

M. p. 170° (from a mixture of alcohol and ether). $[\alpha]_D + 11.8°$ (c 4.412, water).

Found %: Cl 8.28. $C_{18}H_{25}O_7NS \cdot HCl$. Calculated %: Cl 8.15.

Decomposition with cooling of 3 g of the salt with sodium bicarbonate gave 2.5 g of trichodesmine thio-ether with m. p. 151-152° (from alcohol).

Found %: C 54.20; H 6.52; N 3.44; S 7.95. $C_{18}H_{25}O_7NS$. Calculated %: C 54.13; H 6.26; N 3.50; S 8.02.

Catalytic reduction of the hydrochloride of thiotrichodesmine followed by acid hydrolysis gave retronecanol and trichodesmic acid.

Oxidation of trichodesmic acid. 4.53 g trichodesmic acid was added to a solution of 25 g CrO_3 and 35 g sulfuric acid in 500 ml water. The solution was heated 10 hr. The mixture was made alkaline and steam distilled to give 25 ml distillate. Treatment of the latter with benzaldehyde gave dibenzylideneacetone. The residue was acidified and another 1 liter liquid was obtained by steam distillation. Titration of this solution consumed 2.65 g-equiv KOH. The whole of the solution was then evaporated. Acetanilide was obtained from the dry residue by treatment with aniline hydrochloride.

Tetrahydrotrichodesmine was obtained by catalytic reduction of trichodesmine in presence of Raney nickel. M. p. 184° (from anhydrous ethanol). Trichodesmic acid was isolated from the acidified solution of tetrahydro-trichodesmine, and the amino alcohol retronecanol from the alkaline solution.

SUMMARY

1. New alkaloids isolated from the seeds and above-ground portions of Trichodesma incanum (Bge) DC are incanine ($C_{18}H_{27}O_5N$), incanine N-oxide, trichodesmine ($C_{18}H_{27}O_6N$) and trichodesmine N-oxide.

2. Two geometrically isomeric acids are formed by hydrolysis of incanine, depending on the method employed: incanic and isoincanic acids $C_{10}H_{16}O_4$ (V). Incanic acid can be transformed into isoincanic acid and conversely. Reduction of the methyl esters of incanic and isoincanic acids with $LiAlH_4$ gave trihydroxy compounds $C_{10}H_{22}O_3$ (III). Incanic and isoincanic acids are the γ-lactone of 2-hydroxy-3,5-dimethylhexane-2,4-dicarboxylic acid (IV).

3. Incanine (I) has the structure of a cyclic diester of retronecine and 2-hydroxy-3,5-dimethylhexane-2,4-dicarboxylic acid.

4. The structure of trichodesmic acid (VII) was established as the γ-lactonic acid of 2,3-dihydroxy-3,5-dimethyhexane-2,4-dicarboxylic acid (VI). Trichodesmine is the cyclic diester of retronecine and 2,3-dihydroxy-3,5-dimethylhexane-2,4-dicarboxylic acid (II).

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DISCUSSION

CONCERNING THE CAUSES OF TRANSLOCATION OF METALS IN
THE ELECTROCHEMICAL SERIES IN NONAQUEOUS MEDIA

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1. Yu. K. Delimarskii published a paper in the fourth issue of Journal of General Chemistry for 1958 in which he criticized our views on the causes of translocation of metals in the electrochemical series which was based on modern concepts of the structure of liquids. This criticism was based on distortions of our ideas.

According to the well known modern theory of the liquid state, there is a certain degree of ordering in a liquid near the melting point which is reminiscent of order in solids. Some investigators adhere to a quasi-crystalline hypothesis, while others support the microcrystalline hypothesis formerly advanced by G. V. Stuart. Subsequent investigations of the liquid state showed that ordering processes are also observed in solutions. Today there are unlikely to be any opponents of these views. All that remains is to impart more precision to the concepts themselves and to clarify the existing picture. We only resorted to these concepts in order to throw light upon a number of observations made in studies of solutions of electrolytes in solvents with low permittivity (P) and in extremely concentrated solutions in solvents with high P.

2. What is the essence of our views? Investigations of the molecular state of electrolytes in solvents with low P had shown that the molecular weight of these electrolytes is always higher than would be expected on the basis of their chemical formulas, the apparent molecular weight increasing with rising concentration, i.e., the degree of association increasing [1, 2]. At the same time the molar electrical conductivity increases [2, 3]. We interpreted these phenomena in the light of modern teaching on the structure of the liquid state. We started from the fact that in solvents with low P, according to the Coulomb law $F = \dfrac{e^2}{Dr^2}$, the force of attraction between the ions is very much higher than in aqueous solutions under otherwise identical conditions. The ions consequently become associated into groups. We correlated the increase in association with increasing electrolyte concentration with the degree of ordering of the electrolyte in the solution. We regarded these associated groups as structural groups [4]. In order to account for the rise in molar electrical conductivity with increasing concentration, we assumed that the ions in the structural groups do not lose their individuality but participate in the current transfer [5].

3. Are our ideas in harmony with modern teaching on the structure of the liquid state? X-ray investigations of a series of solutions showed that the theory of uniform distribution of molecules of a dissolved substance in solution is not always valid. Some parts of a solution may contain particles of the one component. For example, the work of V. L. Danilov and I. V. Radchenko [6] on the systems Bi–Pb, Bi–Sn, Sn–Pb and Sn–Zn of eutectic composition justified the assumption that in the liquid state these alloys contain small pockets consisting substantially of pure components. The same conclusion was reached by A. F. Skryshevskii [7]. It was shown that eutectic melts of Bi–Pb and Pb–Sn contain regions very closely corresponding in structure to Bi and regions very closely corresponding to Pb and Sn. A similar picture was found in the system acetone–water [8]. These observations are obviously quite at variance with the normal picture of electrolytes in solution. Again, x-ray studies of strong solutions of sodium chloride in water led V. L. Danilov and B. E. Neimark [9] to suggest that "... prior to crystallization the liquid phase contains pockets enriched with molecules of NaCl while other small regions contain a deficiency of such molecules. The latter regions will have

a structure approximating to the structure of pure water." In connection with the development of certain types of atomic configuration (or groups) in solutions or melts, V. I. Danilov writes: "Although associations of like atoms are energetically favored, two types of groups may occur in solutions — one enriched in one component and the other enriched in the second component. The manner of packing of the two types need not necessarily be the same" [10]. In solutions of electrolytes in solvents with a low P, the forces of interaction between ions in the region of low concentrations are equivalent to the forces of interaction of the same ions in concentrated solutions in solvents with large P. This results in an increased degree of association with rising concentrations of the solutions. The presence in solution of structural formations (associates) in an experimentally established fact. It is quite inexplicable why the structural groups formed from dissimilar ions in relatively weak solutions should not be detected in cryoscopic investigations. We do not find any scientific arguments against these pronouncements in Delimarskii's paper. Indirect proof has been obtained of the correctness of our theory that the observed association of an electrolyte in solvents with low P is the result of ordering of the electrolyte. If formation of structural groups in a solution is the result of a certain degree of ordering then the process must conform to the laws of formation of ionic lattices, i.e., the degree of association of the electrolyte must influenced by the properties of the ions, including their polarizability. Experiments have shown that increasing polarizability of ions in accompanied by an increased degree of association of the electrolyte [11]. The experimental results are thus in complete harmony with the theoretical approach. Also not devoid of interest are the speculations of Delimarskii about ordered structures in fused salts. A paper published in 1956 contains this passage "... at a temperature close to the crystallization temperature there appear to be already formed in part in a melt very small (elementary) crystallites, but under these thermal conditions they are easily broken down (!)". This "breaking-down" can go in two directions in melts of electrolytes: a) breakdown of the crystallites leads to neutral molecules which are less associated than the elementary crystallites themselves (?); b) breakdown proceeds in such a fashion as to produce positively and negatively charged particles which are capable of conducting an electric current and of being discharged at electrodes (there will be very few "ordinary" ions under these thermal conditions) [12]. Readers can judge for themselves the extent to which these statements by Delimarskii are scientifically founded and the extent to which they are in accord with what he wrote in his critical paper.

4. In the paper in question Yu. K. Delimarskii wrote: "...'structural groups'possess an intrinsic internal electrical conductivity which is higher than the conductivity exerted by the same ions which do not form'structural groups'; moreover, these are not associates, for the latter do not possess intrinsic internal superconductivity". In none of our papers have we said anything to this effect. We have never written that the internal electrical conductivity of structural groups must be higher than that of the same ions when not forming part of structural groups, nor have we mentioned internal superconductivity. Delimarskii found it necessary to make these statements in order to demonstrate a contradiction between the hole theory of electrical conductivity of ionic lattices and our ideas about the causes of the "anomalous" course of the μ_1 versus φ curves (μ_1 is the molar electrical conductivity corrected for viscosity and φ is the dilution). Let us see if this is so. With increasing concentration of electrolyte in solvents with low P, the molar electrical conductivity rises, often reaches a maximum and then falls. We showed that if the viscosity is taken into account the maximum of the molar electrical conductivity disappears in electrolyte—dielectric systems [5, 13]. Many investigators have shown that an "anomalous" course of the μ_1 versus φ curve is developed when a correction is made for viscosity in the case of the molar electrical conductivity of concentrated solutions in solvents with high P in the region of high concentrations [14]. The universality could thus be demonstrated of the phenomena observed in highly concentrated solutions of electrolytes in solutions with high P, in solutions of electrolytes in solvents with low P, and in fused systems. From this viewpoint the entire diversified range of electrolytic solutions merges into one whole. In order to account for the fall in the viscosity-corrected molar electrical conductivity with dilution, we assume that "free" ions, neutral ions pairs and structural groups are present in the region of concentrations in which this phenomenon is observed; the structural groups characterize the degree of ordering of the electrolyte in solution. The carriers of the current are the "free" ions and the ions constituting the structural groups. In other words these ions do not lose their individuality and they participate in the conduction of the current, i.e. the structural groups possess internal conductivity. With increasing dilution the structural groups break down with formation of a certain number of neutral ion pairs whose ions do not participate in current transfer, i.e., the number of current carriers decreases so that the viscosity-corrected molar electrical conductivity ($\mu \cdot \eta$) falls. Since the decrease in the value of $\mu \cdot \eta$ with dilution is associated with a lesser degree of ordering, increase of the latter must be accompanied by a rise in the viscosity — corrected molar electrical conductivity. But, since the observed degree of ordering of an electrolyte in the liquid phase corresponds to the pure salt, the the
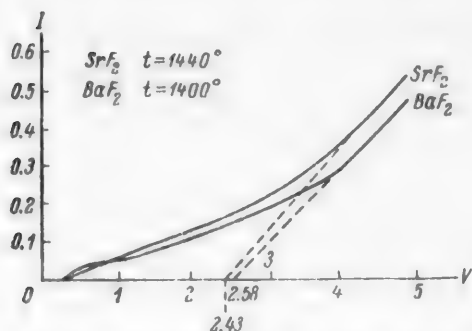
maximum viscosity-corrected molar conductivity should also be observed in the case of the pure liquid electrolyte. This reasoning was found correct for a number of systems. The expected results were fully confirmed by experiments [15]. We did not find a single exception. If all of these ideas are valid, we should expect that with rising temperature the degree of ordering of the electrolyte would decrease and this should lead to a fall in the value of $\mu \cdot \eta$. This is actually observed [16]. These are the facts. Where then does Delimarskii see a "contradiction" between our views and the modern theory of the electrical conductivity of ionic crystals? In the fact that with increasing ordering of the electrolyte in the liquid phase the electrical conductivity should, according to Gorenbein, decrease, while the theory of Ya. L Frenkel'[17] demands the contrary. Firstly, we are considering the dependence of the viscosity-corrected molar electrical conductivity on the dilution, and not electrical conductivity in general (Delimarskii is silent on this point). Secondly, we do not apply the hole theory of the conductivity of ionic crystals to conductivity in the liquid phase. For structural groups we only liken the arrangement of the ions to that of the ions in crystals, but with the proviso that all of the ions of the structural group participate in the transfer of current. It seemed clear that, due to thermal movement, the ions of the structural group are readily mobile and in presence of an electrical field they move in a particular direction. Consequently the increased electrical conductivity with rising temperature is mainly associated with a reduced viscosity of the medium, while the fall in the value of $\mu \cdot \eta$ is bound up with a smaller degree of ordering with formation of neutral ion pairs, leading to a smaller number of carriers of current. Delimarskii mechanically extends the hole theory of the transfer of current in crystalline ionic lattices to melts. But, a closely ordered structure does not fix an ion in a specific position, and the concept of "holes" as empty nodes in an ionic lattice evidently becomes meaningless. Comments on this matter by Ya. L Frenkel' himself are of interest. In connection with fused salts he writes as follows: "Indeed in the absence of nodes in which ions of different signs are assumed to be located, it is meaningless to speak of 'dislocated' ions or of holes (at any rate in the same sense as for crystals). Since in these conditions 'autodissociation' of molecules into ions persists, i.e., the degree of dissociation of the melt remains equal to unity, its electrical conductivity must be governed only by the mobility of ions of different signs, precisely as in the case of weak aqueous solutions of strong electrolytes . . ." [17]. So much for the "contradiction" detected by Delimarskii.

5. On the basis of the foregoing discussion, we can now consider the causes of rearrangement of metals in the electrochemical series in nonaqueous media from the standpoint of the modern theory of the structure of the liquid state. Our views are based on the well-known fact that the concentration of potential-determining ions influences the magnitude of the electrode potential. When complexes are formed, we have to consider which sphere contains the potential-determining ion. If the latter is in the outer sphere, then the theory of structural groups accounts satisfactorily for the change of position of metals in the electrochemical series [18]. Delimarskii has here again distorted our views by assuming that we reject the possibility of complex formation in fused media. He writes: "It is just as erroneous to regard $AlCl_3$ or $AlBr_3$ as dielectrics in the system $KCl-AlCl_3$ or $KBr-AlBr_3$ as to regard SO_3 as a dielectric in the compound K_2SO_4". It is difficult to understand the basis of this argument. We may point out that $AlBr_3$ is a solvent for complexes into whose composition it enters; but when the ratio of the components corresponds to the composition of the complex there is obtained an individual electrolyte, although thermal dissociation may occur. It is well known that $AlBr_3$ is a dielectric, and its P at 100° is 3.375 [19]. The lower the P of solvent the greater the degree of association of the electrolyte. In rejecting the theory of structural groups (associates), Delimarskii writes: "We understand associates to be molecular compounds formed by like molecules". In science, however, we must be prepared to modify established theories. Can one really exlude the possibility of association of unlike ions into groups of ions ? Is not the precrystallized state of electrolytes an association of ions?

It would be impossible to discuss all of the questions touched on in Delimarskii's paper, but we feel compelled to draw attention to the experimental material which is submitted in support of the criticisms. The table presented by Delimarskii shows that the equivalent electrical conductivity of sodium and potassium fluorides is lower than the conductivity of other halides of these metals, whereas in the case of the same degree of dissociation we should expect (on the basis of ionic mobilities) the opposite effect. The point to be noted here is that Delimarskii did not include in his table the equivalent electrical conductivity of lithium fluoride ($\lambda_{LiF} = 258$) and lithium chloride ($\lambda_{LiCl} = 167$) which he had previously cited [20]. It should be noted that the values of λ for fluorides not only deviate from those of other halide ions with a common cation, but also from those of fluorides of alkali metals ($\lambda_{LiF} = 258$, $\lambda_{NaF} = 77.3$, $\lambda_{KF} = 95.5$). The character of their dissociation possibly differs from that of other halides [21, 22]. If Delimarskii had compared the values of conductivity with allowance for the viscosity, then his data would have been relevant to our discussion, but this was not done.

ance for the viscosity, then his data would have been relevant to our discussion, but this was not done.

Special notice should be taken of Delimarskii's claim that his experimental data on electrode potentials in fused fluorides "are in sharp contradiction to Gorenbein's conclusions". Delimarskii set forth the experimental data on electrode potentials in fused fluorides and other halides [12, 20] and "showed" that electrode potentials in flused fluorides are more negative. This is indeed at variance with our findings. But how does Delimarskii find the electrode potentials of metals in fused fluorides? By determination of the decomposition voltage by means of curves I to V. The magnitude of the electrode potential of fluorine is deducted from the results obtained. This seems a dubious procedure. In a recent paper [23] he writes: "Assuming to a first approximation that the electrode potential of fluorine is identical in all of the mixtures of fluorides that we investigated, we calculated the individual electrode potentials of the metals". During the plotting of curves I to V carbides were formed fairly often on the cathode (carbon electrodes were used); some of the metals are in the gaseous state at the experimental temperature and gas is released at the anode; CF_4 is formed. An anodic effect often occurs. Extrapolation to zero current strength, as we see from the adjacent diagram taken from paper [24], is a somewhat arbitrary procedure. It is from such qualitative data that the magnitudes of the electrode potentials were calculated. Values of potentials in different media at the same

Decomposition voltage of SrF_2 and BaF_2 in the fused state.

temperature were calculated with the help of the temperature coefficients $\frac{\Delta E}{\Delta T}$. Such a calculation has no justification since the temperature range is several hundred degrees, while the temperature coefficients alter with rising temperature and the order in which metals are arranged in the electrochemical series changes with rising temperature. Examples of the alteration of the order of arrangement of metals in the electrochemical series in melts with rising temperature are cited by Delimarskii [25]. It is quite obvious that these data cannot be comparable and therefore cannot serve as a basis for the development of a theory. We must also draw attention to the technique for plotting curves I to V of the fused fluorides.

Figure 1 in paper [24] is a representation of the graphite block of the crucibles serving as containers during the plotting of curves I to V. Both of the spaces communicate through a diaphragm with a 1 mm diam. hole. This diaphragm is evidently a bipolar electrode, and the hole would be unlikely to alter the nature of the phenomenon. This experimental setup for the plotting of curves I to V excludes the possibility of obtaining trustworthy results. The numerical values obtained by this procedure should be multiplied by two since curves I to V were actually plotted with two cells in series.

We think we have refuted Delimarskii's observation that the ideas of Gorenbein "are in conflict with a large number of facts".

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A NEW EMPIRICAL EQUATION FOR THE RADII OF IONS WITH AN INERT GAS ELECTRONIC STRUCTURE

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The magnitude of the effective radii of ions depends on the type of bond in the crystal, on the coordination number of the crystal structure, and on the chemical nature of the ions that surround the ion in question. The radii of ions are constant for a given type of bond and a given coordination number (to within several percent) and do not depend on other components of the compound. To a first approximation we can say that the distance between ions in a crystal is equal to the sum of the radii ($d = r_k + r_a$). Goldschmidt [1] made use of the numerical values of the radii of O^{2-} and F^- found by Wasastjerna [2] on the basis of experimental data for the interatomic distances (d), and calculated therewith the radii of the majority of ions. The resulting empirical system of Goldschmidt is used for comparisons of radii calculated with the aid of various equations.

Pauling [3] was the first to attempt a theoretical calculation of the radii of ions, and later Jensen, Meyer-Gossler and Rohde [4] calculated the radii of ions of alkali metals and halogens. These were based on semi-empirical methods. Other, completely empirical, equations were also proposed which link ionic radii with a physicochemical constant — most usually the atomic number of the element [5-8]. Finally, according to [9] the ionic radius is a function of the total number of electrons (m) in the ion and of its valence (η). The proposed formula $r = \dfrac{\log m}{\eta^{1/3}}$ relates only to cations containing 8 electrons in the outer layer.

In the present short note, we wish to demonstrate that Kapustinskii's equation [9] is a special case of a more general empirical equation:

$$r = a + k \log Z, \tag{1}$$

where $\underline{k}$ is a constant, $\underline{a}$ is a function of the valence of the ion, and Z is the atomic number of the element.

This expression is valid both for cations and for anions with inert gas structure. By means of equation (1) we can also calculate the radii of ions whose magnitude has not been experimentally established. The proposed expression may be used for calculation of certain magnitudes which are functions of the radius of ions. •

To a first approximation the coefficient $\underline{k}$ can be assumed equal to unity for cations. More accurately, its value is 0.95. This result is not unexpected. Conversely, we can expect that even for different groups of the periodic system the coefficient will have similar but not identical values. This is found to be the case. The equation can also be written in the form:

$$r = k (a' + \log Z), \tag{2}$$

where $a' = a/k$. This new constant is a simple function of the valence of the cation, namely $a' = (1 - n)/4$, where $\underline{n}$ is the valence of the ion.

•The equation may be used, for example, to demostrate the inapplicability of the thermochemical logarithmic rule in the region of the heats of hydration of ions [10, 11].

The coefficient k is not a constant for anions but a function of the valence of the anion. For example, for univalent anions $k = 1.10$, and for divalent anions $k = 0.95$. Here a is equal to $\log (1 + n)$ where n is the valence of the anion.

Radii of Ions with Inert Gas Electronic Structure

Ion	Radii of ions (in A) calculated according to						
	[1]	[2]	Δ	[13]	Δ	from equation (2)	Δ
Na^+	0.98	0.95	0.03	1.00	−0.02	0.99	−0.01
K^+	1.33	1.33	0.00	1.26	0.07	1.21	0.12
Rb^+	1.49	1.48	0.01	1.56	−0.07	1.49	0.00
Cs^+	1.65	1.68	−0.03	1.73	−0.08	1.65	0.00
Be^{2+}	0.34	0.31	0.03	—	—	0.33	0.01
Mg^{2+}	0.78	0.65	0.13	0.79	−0.01	0.79	−0.01
Ca^{2+}	1.06	0.99	0.07	1.00	0.06	1.00	0.06
Sr^{2+}	1.27	1.13	0.14	1.24	0.03	1.27	0.00
Ba^{2+}	1.43	1.35	0.08	1.38	0.05	1.43	0.00
B^{3+}	0.20	0.20	0.00	—	—	0.19	0.01
Al^{3+}	0.57	0.50	0.07	0.69	−0.12	0.58	0.01
Sc^{3+}	0.83	0.81	0.02	0.87	−0.04	0.78	0.05
Y^{3+}	1.06	0.93	0.13	1.08	−0.02	1.04	0.02
La^{3+}	1.22	1.15	0.07	1.20	0.02	1.20	0.02
Si^{4+}	0.39	0.41	−0.02	0.63	−0.24	0.38	0.01
Ti^{4+}	0.64	0.68	−0.04	0.79	−0.15	0.56	0.08
Zr^{4+}	0.87	0.80	0.07	0.98	−0.11	0.81	0.06
Ce^{4+}	1.02	1.01	0.01	1.09	−0.07	0.96	0.06
F^-	1.33	1.36	−0.03	—	—	1.35	−0.02
Cl^-	1.81	1.81	0.00	—	—	1.65	0.16
Br^-	1.96	1.95	0.01	—	—	1.99	−0.04
I^-	2.20	2.16	0.04	—	—	2.20	0.00
O^{2-}	1.32	1.40	−0.08	—	—	1.33	−0.01
S^{2-}	1.74	1.84	−0.10	—	—	1.62	0.12
Se^{2-}	1.91	1.98	−0.07	—	—	1.91	0.00
Te^{2-}	2.11	2.21	−0.10	—	—	2.09	0.02

Values for the radii of different ions calculated with the help of the above equation are set forth in the table and compared with the empirical radii calculated from Goldschmidt's relation, with those theoretically calculated by Pauling and with the data obtained with Kapustinskii's equation. It is clear that, with the exception of elements of the fourth period (containing 18 electrons), the results are in very good agreement with the empirical radii of Goldschmidt.

By means of our proposed equation we can calculate the radii of ions of the seventh period – Fr^+, Ra^{2+}, Ac^{3+} and Th^{4+} (there are no experimental data for some of them), as well as the radii of At^- and Po^{2-}. The results, however, are too high. This is probably because the radii of ions depend not only on the structure of the outer shells but also on that of the inner electron shells. Starting from $Ce(Z = 58)$. and proceeding to Lu ($Z = 71$) there occurs an addition to the inner 4f shells, whereas the outer electron layers remain unchanged. Due to this, the radii of ions and atoms of lanthanides become smaller (the "lanthanide contraction"). Decrease in radii (both of atoms and of electrons) is also observed with elements whose atomic number is greater than 72. Therefore, all ions whose atomic number is higher than 72 will have radii smaller than those calculated from equation (2). It may be suggested that the error in calculation of the ionic radii of elements of the seventh period will be smaller if Z in equation (2) is replaced by $Z - 14$, i.e., if we deduct from the atomic number of these ions a number equal to the number of 4f electrons. The following results are obtained when utilizing the so-corrected equation for calculation of radii: For Fr^+ (no experimental data available) our equation gives a radius of 1.77 A, which is in good agreement with that calculated by Ahrens [8] and Yatsimirskii [14] (1.80 A) but very different from the results of Kordes [5] and Kapustinskii [9] (1.90 A). For Ra^{2+} we obtain a radius of 1.54 A. According to Kapustinskii the value is also 1.54 A, but according to Schulze [15] it is 1.52 A. For Ac^{3+} our equation leads to a radius of 1.31 A which differs from the experimentally found radius by 0.03 A. The

value obtained for Th^{4+} (1.07 A) also agrees with the experimental value (1.10 A) but differs considerably from the value found by Kapustinskii (1.20 A). For At^- we obtain a value of the radius of 2.34 A, and for Po^{2-} 2.23 A.

By means of the method of least squares we can demonstrate that the proposed equation is very good agreement with experiment. For this purpose we sum the squares of the difference between the calculated and the experimental magnitudes. The sum of the squares of the errors for radii calculated with equation (2) are lower than for values calculated on the basis of other proposed equations. For example, by our equation we obtain 355×10^{-4} A^2, while Kapustinskii's equation gives 1376×10^{-4} A^2.

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LETTERS TO THE EDITOR

THE SYNTHESIS OF MONO- AND DIKETONES OF THE TETRAHYDROPYRAN SERIES FROM 3-FURANIDONES AND 3,4-FURANIDINEDIONES

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In continuation of our preceding studies [1] on the synthesis and properties of ketones of the tetrahydrofuran series, we have investigated the reactions of 2,2,5,5-tetraalkyl-3-furanidones and of 2,2,5,5-tetraalkyl-3,4-furanidinediones with diazomethane. We found that in both cases the ring is enlarged with formation of tetrahydro-3-pyrones and of methyl ethers of tetrahydro-3,5-pyrandiones respectively.

For example the reaction of an ethereal solution of 7.2 g diazomethane (21% excess) with 20 g 2,2,5,5-tetramethyl-3-furanidone in ether in presence of methanol (20°, 3 days) gave 3.95 g 2,2,6,6-tetramethyltetrahydro-3-pyrone (39.5% yield on the ketone reacted and 18% on the ketone taken into reaction).

B. p. 62-63° (9 mm), $n^{20}D$ 1.4413, d^{20}_4 0.9529, MR_D 43.32; calc. 43.22.
Found %: C 69.20, 69.26; H 10.49, 10.44. $C_9H_{16}O_2$. Calculated %: C 69.19; H 10.32.

Semicarbazone: m.p. 197-198°.
Found %: N 19.53, 19.73. $C_{10}H_{19}O_2N_3$. Calculated %: N 19.70.

Traces of 2,2,6,6-tetramethyltetrahydro-4-pyrone are also formed; semicarbazone with m. p. 219-220° (decomp.)(from water). Literature: m. p. 212° (decomp.) [2].
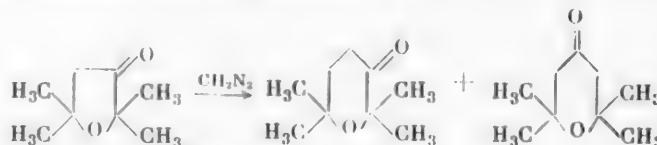
When diazomethane acts on 2,2,5,5-tetraalkyl-3,4-furanidinediones, the β-diketones resulting from ring enlargement are methylated by the diazomethane to give methyl ethers of 2,2,6,6-tetraalkyltetrahydro-3,5-pyrandiones. By this route, for example, treatment of 7.8 g 2,2,5,5-tetramethylfuranidine-3,4-dione with an ethereal solution of diazomethane (from 27.5 g nitrosomethylurea) for 1 hr at 0° led to 4.1 g (44.5%) methyl ether of 2,2,6,6-tetramethyltetrahydropyran-3,5-dione with m.p. 74-75° (after sublimation in vacuo).

Found %: C 65.26, 65.20; H 8.79, 8.93. $C_{10}H_{16}O_3$. Found %: C 65.19; H 8.75.

Oxime: m. p. 116.5°.
Found %: N 7.36, 7.46. $C_{10}H_{17}O_3N$. Calculated %: N 7.03.

Hydrolysis of 1.02 g of this ether with 10% hydrochloric acid at 100° for 1 hr gave 0.87 g (92.5%) of 2,2,-6,6-tetramethyltetrahydropyran-3,5-dione with m. p. 158-158.5° (from a mixture of benzene and ligroine followed by sublimation in vacuo). Soluble in alkalies.

Found %: C 63.31, 63.51; H 8.42, 8.54. $C_9H_{14}O_3$. Calculated %: C 63.51; H 8.29.

Dioxime: m. p. 160-161° (decomp.).
Found %: C 54.02, 54.14; H 8.00, 8.19; N 14.08, 13.86. $C_9H_{16}O_3N_2$. Calculated %: C 53.98; H 8.06; N 13.99.

The diketone is obtained in 66% yield if the methyl ether of 2,2,6,6-tetramethyltetrahydropyran-3,5-dione, resulting from the action of diazomethane on 2,2,5,5-tetramethylfuranidine-3,4-dione, is immediately subjected to hydrolysis without preliminary isolation and purification being undertaken. Methylation with diazomethane gives an ether identical with that described above.
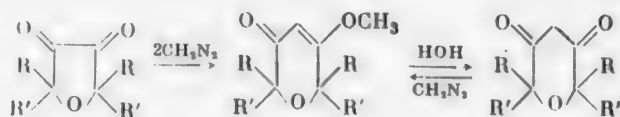

The only analogous reaction course of an α-diketone with diazomethane noted in the literature is that of camphorquinone [3].

Heating of 0.34 g 2,2,6,6-tetramethyltetrahydropyran-3,5-dione with 0.21 g benzaldehyde (2 hr at 100°) in pyridine in presence of a trace of piperidine gave 0.39 g (91%) phenyldi-(2,2,6,6-tetramethyltetrahydropyran-3,5-dione-4-yl)-methane with m. p. 123-125°.

Found %: C 70.11, 70.25; H 7.53, 7.72. $C_{25}H_{35}O_9$. Calculated %: C 70.05; H 7.53.

Azocoupling of 0.34 g diketone with p-nitrophenyldiazonium chloride gave 0.58 g (90.5%) 4-p-nitrophenyl-hydrazone of 2,2,6,6-tetramethyltetrahydropyran-3,4,5-trione with m. p. 181-182° (from dilute alcohol).

Found %: C 56.56, 56.51; H 5.59, 5.61; N 13.27, 13.43. $C_{15}H_{17}O_5N_3$. Calculated %: C 56.42; H5.37; N 13.16.
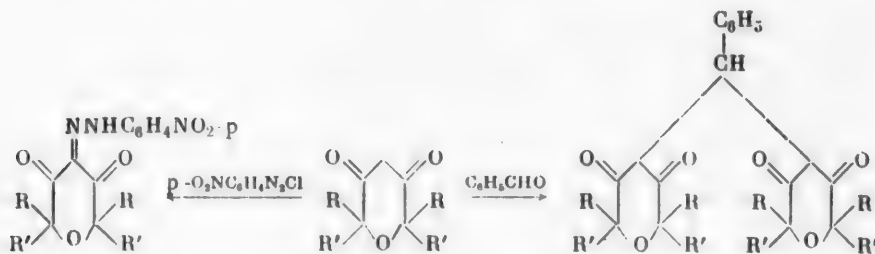
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THE MAGNETIC SUSCEPTIBILITY OF TROPYLIUM SALTS

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It was recently shown by experiment [1] that the compound C_7H_7 is stable in the form of the positively charged $C_7H_7^+$ ion with a cyclic structure. Interest is attached to the determination of diamagnetic susceptibility of this ion and to the comparison of the result with the susceptibility of other cyclic molecules such as benzene and cyclooctatetraene. With this objective we synthesized tropylium hexachloroplatinate $(C_7H_7)_2 PtCl_6$ tropylium perchlorate $C_7H_7ClO_4$, and tropylium mercuritetraiodide $(C_7H_7)_2HgI_4$. We also measured their susceptibilities.

The method of preparation of the first two compounds has already been described [2]. Tropylium mercuritetraiodide has now been obtained for the first time in the following manner: 2.34 g C_7H_7Br was dissolved in 10 ml water and to the solution were added an aqueous solution of $HgCl_2$ (twofold excess, 3.72 g) and 9.1 g KI. The orange-red precipitate of $(C_7H_7)_2HgI_4$ was filtered, and washed with 10% KI solution, water and alcohol. After drying in vacuo, the compound was recrystallized from hot nitromethane.

The red crystals melted at 175-175.5°.

Found %: C 18.68, 18.80; H 1.55, 1.56; Hg 22.60, 22.34; I 56.97, 57.38. $(C_7H_7)_2HgI_4$. Calculated %: C 18.88; H 1.58; Hg 22.53; I 57.01.

The magnetic susceptibility was determined by Sacksmith's method at room temperature using a weak magnetic field. Results are presented in the table. It should be noted that tropylium hexachloroplatinate differs from other platinates in that its susceptibility varies for products of different batches. The highest absolute value of the susceptibility is given in the table; it probably corresponds to the magnetically purest specimen.

Magnetic Susceptibility of Tropylium Compounds

Compound	Magnetic susceptibility $(-\chi \cdot 10^6)$			
	γ_G	γ_M	χ anion	$\chi_{C_7H_7^+}$
$(C_7H_7)_2PtCl_6$	0.423	250	147	51
$C_7H_7ClO_4$	0.466	89	34	55
$(C_7H_7)_2HgI_4$	0.376	335	236	50

We tried to calculate the magnetic susceptibility of the tropylium cation $C_7H_7^+$ from the experimental data. This necessitated deduction of the values for the respective anions from the molar susceptibility of the salts. The susceptibilities of the anions are listed in the fourth column of the table. In order to find the susceptibility of $PtCl_6^{2-}$ we made use of our previously published [3] values of the susceptibilities of the chloroplatinates of sodium, potassium and ammonium. For the susceptibility of the HgI_4^{2-} ion we used data for the susceptibility of Na_2HgI and K_2HgI_4 [4]. The susceptibility of the ClO_4^- ion was taken from Table 3 of Selwood's book [5].

The susceptibility of the $C_7H_7^+$ ion, found from the various tropylium compounds, is shown in the last column of the table. The mean value of $\chi_{C_7H_7^+}$ is $(52 \pm 2) \cdot 10^{-6}$, i.e. lower than for benzene which has a susceptibility of $55 \cdot 10^{-6}$.

We know that Pascal's additive scheme is inadequate in the case of compounds containing conjugated bonds, e.g. C_6H_6, $C_7H_7^+$ and C_8H_8. According to Pascal, on passing from C_6H_6 to C_7H_7 the additional CH group should cause a rise in the absolute value of susceptibility of 9.4×10^{-6}, thus giving the value of 64.4×10^{-6}. On the other hand, however, the transition to a positive ion leads to a lower value since we know that positive ions have a lower absolute value of diamagnetism than the corresponding isoelectric inert gases.

Lowering may be caused by lowering of the value of the term $\dfrac{Ne^2}{6m_0c^2} \sum r_0^2$. At the same time the term i in the general equation representing the paramagnetic polarizability of the molecule is increased We may note that cyclooctatetraene, C_8H_8, which contains four double bonds but whose conjugation is diminished by the absence of coplanarity, has a susceptibility of 51.9×10^{-6} [6], i.e. again lower than that of benzene. This indicates that double bonds carry a considerable paramagnetic charge.

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*Original Russian pagination. See C.B. Translation.

SYNTHESIS OF HETEROORGANIC COMPOUNDS WITH THE GENERAL FORMULA $Me^n[OSiR_3]_n$

B. I. Yakovlev and N. V. Vinogradova

Interest has recently developed in investigations of new heteroorganic compounds containing silicon together with atoms of other elements. We are therefore presenting the results of investigations on the synthesis of compounds of the general formula $Me^n[OSiR_3]_n$ which we carried out in 1949-1952 [1].

We prepared tetra[triethylsilyl]titanate (in yields of up to 60%) by transesterification of tetraethyl orthotitanate with excess of triethylsilanol.

$$Ti(OC_2H_5)_4 + 4(C_2H_5)_3SiOH \rightarrow Ti[OSi(C_2H_5)_3]_4 + 4C_2H_5OH$$

Tri[triethylsilyl]borate was synthesized (in a yield of up to 40%) by reaction of triethylsilanol and boron trioxide in presence of anhydrous copper sulfate.

$$B_2O_3 + 6(C_2H_5)_3SiOH \rightarrow 2B[OSi(C_2H_5)_3]_3 + 3H_2O$$

Organosilicophosphorus compounds of the formulas $P[OSiR_3]_3$ and $PO[OSiR_3]_3$ were synthesized by the procedure developed by A. E. Arbuzov for the preparation of organic esters of phosphorus acids [2]. Tri[triethylsilyl]phosphite and tri[triethylsilyl]phosphate were synthesized by the action of phosphorus trichloride (or oxychloride) on sodium triethylsilanolate.

$$3(C_2H_5)_3SiONa + PCl_3 \rightarrow P[OSi(C_2H_5)_3]_3 + 3NaCl$$

$$3(C_2H_5)_3SiONa + POCl_3 \rightarrow PO[OSi(C_2H_5)_3]_3 + 3NaCl$$

Tri[triethylsilyl]phosphite was produced in 45% yield; yield of tri[triethyl]phosphate was 34%.

EXPERIMENTAL

Preparation of tetra[triethylsilyl]titanate. 6.5 g tetraethyl orthotitanate and 19.6 g triethylsilanol were taken; 8.3 g of product was obtained:

B. p. 199-202° (3.5 mm), $d^{20.5}_4$ 0.917; ϵ at 10^3 cps (20°) 2.18.
Found %: Si 19.47; Ti 8.45; H 10.96. M 586.4. $C_{24}H_{60}O_4Si_4Ti$. Calculated %: Si 19.58; Ti 8.36; H 10.56. M 572.8.

Preparation of tri[triethylsilyl]borate. 2 g boron trioxide and 25 g triethylsilanol were taken; 9.2 g product was obtained

B. p. 152-154° (3 mm), d^{18}_4 0.8962, $n^{21}D$ 1.4375.
Found %: Si 20.58; C 52.65; H 10.55. M 407.0. $C_{18}H_{45}O_3Si_3B$. Calculated %: Si 20.81; C 53.45; H 11.21. M 404.5.

Preparation of tri[triethylsilyl]phosphite. 34 g triethylsilanol, 4 g metallic sodium and 6.8 g phosphorus trichloride were taken; 9.3 g of product was isolated.

B. p. 164-166° (3 mm), d^{18}_4 0.9308, $n^{21}D$ 1.4518.

Found %: Si 19.70; P 7.13. M 423.0. $C_{19}H_{45}O_3Si_3P$. Calculated %: Si 19.83; P 7.29. M 427.7.

Preparation of tri[triethylsilyl]phosphate. 30 g triethylsilanol, 4.5 g metallic sodium and 8.55 g $POCl_3$ were taken; 8.4 g of products was obtained.

B. p. 181-183° (3 mm); $d^{20.5}_4$ 0.9658, $n^{21}D$ 1.4460.
Found %: C 48.29; H 10.12; Si 18.86. M 441.6. $C_{19}H_{45}O_4Si_3P$. Calculated %: C 49.06; H 10.29; Si 19.11. M 440.7.

The authors convey their thanks to M. M. Koton for his guidance and valuable advice.

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The data contained in this letter
were submitted by the authors
in December 1954

ERRATA

A paper by E. A. Nikitina and E. V. Buris was published in 1956 in Journal of General Chemistry on "Thermographic investigation of the most important saturated heteropoly acids" [26, 717 (1956)] which contained a printing error. On p. 718, 16th line from bottom is printed: "The loss of 9 molecules of water of crystallization took place at 109°; at this temperature the acid existed in the form of the hydrate $H_7[P(W_2O_7)_6] \cdot H_2O$". This should read: "The loss of 9 molecules of water of crystallization took place at 109°; at this temperature the acid existed in the form of $H_7[P(W_2O_7)_6] \cdot 4H_2O$".

SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY
ENCOUNTERED IN SOVIET CHEMICAL LITERATURE

Abbreviation (Transliterated)	Significance
FIAN	Phys. Inst. Acad. Sci. USSR
GIPKh	State Institute of Applied Chemistry
GIREDMET	State Rare Metals Scientific Research Institute
GITI	State Sci.-Tech. Press
GITTL	State Tech. and Theor. Lit. Press
GLAVKhIM	Main Administration of the Chemical Industry
GOI	State Optical Institute
GONTI	State United Sci.-Tech. Press
Goskhimizdat	State Chem. Press
GOST	All-Union State Standard
Gostoptekhizdat	State Scientific and Technical Publishing house of the Petroleum and Mineral Fuel Industry
GTTI	State Tech. and Theor. Lit. Press
IFKhA	Institute of Physicochemical Analysis
IL	Foreign Lit. Press
IOKhAN	Institute of Organic Chemistry of the Academy of Sciences of the USSR
IONKh	Institute of General and Inorganic Chemistry (N. S. Kurnakov)
IONKhAN	Institute of General and Inorganic Chemistry of the Academy of Sciences of the USSR
INBI	Institute of Biochemistry
IREA	Institute of Chemical Reagents
ISN (Izd. Sov. Nauk)	Soviet Science Press
IVKhTI	Ivanovo Chemical Engineering Institute
Izd. AN SSSR	Acad. Sci. USSR Press
Izd. MGU	Moscow State Univ. Press
KEIN	Colloid Electrochemical Institute
Khimizdat	Chemistry Press
LGU	Leningrad State University
LIM	Leningrad Institute of Metals
Metallurgizdat	Metallurgy Press
MITKhT	Moscow Institute of Fine Chemical Technology
OIYaI	Joint Institute of Nuclear Studies
OKhN	Division of Chemical Science
ONTI	United Sci.-Tech. Press
OTI	Division of Technical Information
OTN	Division of Technical Science
RIAN	Radium Institute, Academy of Sciences of the USSR
RZhKhim	Chemical Abstract Journal (USSR)
VKhO	All-Union Chemical Society (Mendeleev)
ZhFKh	Journal of Physical Chemistry (USSR)
ZhRKhO	Journal of the Russian Chemical Society

Note: Abbreviations not on this list and not explained in the translation have been transliterated no further information about their significance being available to us. — Publisher.
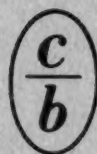
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